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Published for The Scientific and Technical Group of the Royal Photographic Society

edited by R. J. Cox

March 1973, xii+340 pp., £6.00

This book comprises papers delivered at a symposium on Photographic Processing held at the University of Sussex in September 1971.

All the processing systems discussed involve silver halide material which has been the most popular since Fox-Talbot's invention of wet processing 150 years ago.

Much of the conference was occupied with discussing ways of improving colour processing. Methods were suggested for allowing more rapid development, providing more stable colours and making techniques more acceptable to the environment by producing less toxic waste and recovering scarce resources.

Image Processing and Computer-Aided Design in Electron Optics

edited by P. W. Hawkes

April 1973, x+442 pp., £6.50

This book deals with two major innovations in electron optics in recent years—the practical exploitation of wave optics and the deep involvement of the computer in design problems. Parts One and Two are concerned with electron optical contrast transfer theory and with scattering and image formation, while Part Three covers computer-aided design and improvement of the instruments to which the wave theory of imaging is now being applied. Since most of those who have made important contributions to the subject have written chapters for the book it will serve as an authoritative and up to date account of electron image formation and electron lens design.

Human Chromosomes

E. H. R. Ford

March 1973, xiv+382 pp., £7.00

This is a book for everyone interested in human chromosomes. Dr. Ford has collected recent observations and offers some original comments on structure, morphology, identification, behaviour at mitosis and meiosis, and chromosomal abnormalities in man and their transmission. As far as possible the work is based on observations and experiments on human material. Special emphasis is laid on meiotic studies, the new fluorescent techniques for identifying chromosomes are described, and illustrations of karyotypes are given. The final chapter, by Dr. J. H. Renwick, gives an account—unobtainable elsewhere—of recent advances in chromosome mapping in man.

Bone Behaviour

Kitty Little

April 1973, xvi+464 pp., £8.00

There has been a rapid increase recently in our knowledge of bone, and the manner in which the functions of bone and bone marrow are co-ordinated with activities of other tissues and organs, both in health and in disease. This book provides a coherent account of the properties of cells and vessels in bone, tracing the mechanisms of growth and development, the formation and activity of bone tissue and bone marrow, and the effects on these of physical and biological stresses. Particular attention has been paid to such topics as the mechanisms of action of hormones and steroids, osteoporosis and the stress diseases, osteosarcoma and the effects of radiation on bone.

The Mathematics of Finite Elements and Applications

edited by J. R. Whiteman

April 1973, approx. 520 pp., £12.50

This book brings together under one cover thirty-two papers originally presented at the conference on the Mathematics of Finite Elements and Applications held at Brunel University, Uxbridge, England, between 18th and 20th April, 1972.

Four of these thirty-two papers on the mathematical theory of finite elements, their applications, algorithms and computational techniques are expository. The remainder, being papers contributed to the Conference, report on recent research and were selected so that as wide a range of applications as possible is covered.

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BOOK REVIEW SUPPLEMENT

2955

Tomorrow's chromatograph today

How Not to Plan for the Future

THE Conservative government is having bad luck with its attempts to make important decisions about important planning questions. For months now, it has been snarled in endless arguments about the rights and wrongs of the Roskill Commission, the *ad hoc* organization which eventually recommended that the third London Airport should be at Cublington, not Stansted (see *Nature*, **228**, 1241 ; 1970), and whose advice had eventually to be overridden in favour of a deserted stretch of mud in the Thames estuary. Last week, Mr Geoffrey Ripon, Secretary of State at the Department of the Environment, found himself having to decide whether or not to accept the recommendations of a similarly ambitious planning inquiry—the Layfield examination of the Greater London Council's proposals for the development of London—and having to decide that very little profit could be derived from a process of inquiry the report of which boasts—and it is the only boast that can be sustained—that it has been the most expensive so far. The Layfield report is the outcome of a year's hard work by half a dozen distinguished people. The cost is estimated to be in excess of a million pounds. The report and the appendices thereto, mostly a list of documents which diligent readers could procure at further cost, is on sale in shoddy mimeograph for £10. For practical purposes, nothing that it says is convincing. Not merely is it fair to say that the inquiry need never have been held but that this embarrassing outcome raises all kinds of questions about the ways in which governments like the British set out to determine crucial issues of public policy concerned with amenity.

The Greater London Council, itself a newcomer on the scene and a successor to the London County Council of the early 1960s, has been an entirely suitable fall guy for the Layfield exercise. The special importance of London as an international centre as well as a metropolis has necessarily directed special attention to the local authority's proposals for the definition of a planning strategy. In December 1969, the Labour government agreed that special arrangements should be made for a public inquiry into the Greater London Development Plan which the Greater London Council had been required, in 1963, to draw up and which it eventually submitted six months late in August 1969. Few will be surprised that the Greater London Council's view of the future was little better than a crude extrapolation of the past. The council originally put forward what amounts to a passive acceptance of recent trends—the tendency of people living in the inner city to emigrate to the suburbs and their tendency then to travel to work by automobile and their unwillingness to rely on a public transport system geared to move lots of people at peak hours but also to be an inconvenient way of getting about at other times. In 1969, in other words, the Greater London Council was apparently happy with the notion that the city centre should continue to lose people and was most exercised to discover some means of enabling them to travel diurnally to and from

their work. The result was that the Greater London Development Plan consisted chiefly of proposals for building roads where people used to live and only after the inquiry began did the GLC, repentance for irrationality less evident than a concern for rateable values, suggest that its proposals should be amended so as to encourage a less rapid drift of people from the city.

Those who believe that sportsmen should not shoot sitting ducks will despise what the Layfield report has to say about the Greater London Development Plan. The august and hard-working committee of inquiry is right to say that the plan is over-ambitious—to pretend that it is possible to predict for several decades ahead what will happen to the movement of population or the disposition of industry is a little like trying to predict what will be the next great innovation in technology--the trouble is that the hapless Greater London Council was required to do no less by the Town and Country Planning Act of 1947 and 1968. It is also easy to say that the plan was inconsistent—for better or for worse, British governments have found it necessary to agree that the Greater London area should be a single planning unit but that much smaller parts of this vast concentration of people, the London boroughs and the outlying counties, for example, should be politically autonomous. Is it any wonder that a planning authority should find itself unable to reconcile the conflicting interests of its constituents with its own grand vision of the future?

The Layfield committee has great fun with the Greater London Council's failure "to relate information to policies", but that is not surprising. The committee says that "one of the most notable features of the Greater London Development Plan is the independence of the policies in the plan from the facts gathered . . ." and it says that "in many cases we had the greatest difficulty in seeing why the facts led to the solution set forth in the plan . . . and in some cases . . . we never found out at all". What the committee has in mind is the Greater London Council's attachment to ideologies such as the Green Belt or its political awareness of its impotence in the face of the conflicting interests of the Greater London Council's constituents. But might it not have been more cogent, or at least more sporting, to have complained at the planning legislation and not to have taken pot shots at that sitting duck, the Greater London Council? To be sure, it is fair to say that the council has consistently failed to relate its planning policies to its philosophical objectives. But the plain truth must surely be that the council is prevented not merely by its constitution as a federal body, by its existence as an inheritor of previous shibboleths such as the Green Belt and by its awareness that radical proposals might jeopardize its own survival, from being anything but a temporizing institution, ill equipped to face the future but constitutionally unconvinced that there will be one.

The most famous and notorious part of the original development plan was that proposing three rings of motor-

ways around London intended both to help commuters get to work and traffic happening to pass nearby from travelling through congested parts of London. Understandably, people who live in London have for several years been up in arms at the prospect that their houses will be destroyed to make way for motorways or that their favourite patches of greenery will be despoiled. The Layfield report might have said, but it has not done so, that the Greater London Council has consistently failed to demonstrate that its proposals for building motorways were in some sense or another optimum solutions to a difficult problem and even that the motorways would be socially beneficial in the widest sense, balancing economic benefit against social disbenefit. Innocent readers of the Layfield report will look in vain for the kinds of arguments, inevitably somewhat mathematical or just plain arithmetical, that might have thrown light on this important question. Instead, what they will discover is that Layfield and his men, like conjurers pulling rabbits out of hats, has struck out parts of the motorway system which they consider to be unnecessary, have confirmed that other parts should be built, and, in doing so, have given the impression that the chief defect of the Greater London Development Plan is not its conception but its particular choice from the several somewhat arbitrarily balanced alternatives with which it was presented. To be sure, there are plenty of platitudes about the need to encourage travel by public transport, the modern equivalent of the fondness of the 1950s for motherhood, but the ingredients are much the same.

If, among sportsmen, it is agreed that sitting ducks are not fair targets, so it should be acknowledged that sportsmen should not be shot at while unable to defend themselves, which is why Mr Geoffrey Rippon's commentary on the Layfield terms is also tantamount to taking a mean advantage. He says that there is probably much to be said for the Layfield report's belief that a more rapid reduction in the population of London than the Greater London Council is happy about could easily be stomached but asks whether it can be right that the rate of building in satellite towns should be increased and whether the Layfield committee can be right in thinking that high density development should be avoided but that the council should also take steps to avoid the under-use of land, thus making still more uniform the distribution of people within the Inner London area. The trouble, of course, is that it takes only a minor Solomon to make such a comment. Constitutionally, Mr Rippon and his predecessors invited the Greater London Council to say what they would like, then invited the Layfield committee what it thought of what the Greater London Council had said: so vast are the uncertainties that it needs not a senior cabinet minister but only a schoolboy to say that there are grounds for disbelieving both opinions. It is in exactly this spirit that Mr Rippon makes his own amendments to the proposals for road building in London as originally advocated by the Greater London Council and then amended by the Layfield committee.

What is the moral? First of all, there must now be serious doubts of the wisdom of entrusting professional planners with planning. If wars are too important to be left to the generals, is it sensible that people should allow disinterested professionals to decide how people must live? For the truth is that planning is not and never can be a strictly technical question. It is a political matter,

and what the government must decide is not how best to do the local authority's job but rather how to define its own relationship with London planning authorities in such a way that they will be able to do their job efficiently. The worst feature of the whole Layfield episode is not the abysmally unquantitative characteristics of the committee's report but the fact that, having created a planning authority, the government (or, more strictly, its predecessor) decided to do the job itself. The second complaint against this tawdry happening is that none of the three parties to the argument, the Greater London Council, the Layfield committee and the government, has been able to lift its vision above the solutions to familiar problems with which town planners have been wrestling for decades. Why does none of these vast and expensive documents consider other kinds of solution to the problem of living sensibly in cities such as London? In all kinds of ways, it might be better to abandon the Green Belt for the sake of having a city in which people were closely connected together but also with the countryside, possibly in a cellular kind of city. Ultimately, the failure to be imaginative must be blamed on the government, for that is the level to which planning authority has been usurped. Luckily, but ironically, the outcome of the Layfield report is unlikely to be permanent: there is at least a chance that by having approved the plan to build motorways in central London, the government will have so alienated opinion in the city that the Conservative Greater London Council will be defeated by its Labour opponents in May, whereupon the whole issue of the Greater London Development Plan will be put back another decade. This may not be progress, but it is a kind of justice.

100 Years Ago
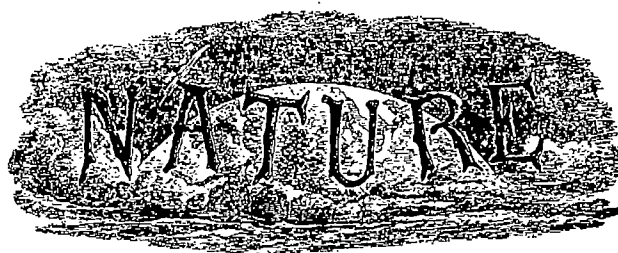
WHEN is the foundation-stone of our grand new Natural History Museum to be laid? Is Government waiting for the advent of fine weather in order that the ceremony may be as auspicious and imposing as possible? We can hardly believe the current gossip that the fiscal authorities of the country have quietly retired the thousands said to have been voted for the purpose, in order that a saving might be effected in their expenditure, and a handsome surplus be vaunted of in the forthcoming budget. Meanwhile see what our young, energetic, long-headed cousins on the other side are doing. A new Natural History Museum is about to be erected in New York 800 feet long by 600 wide, which will be the largest building in America. 100,000*l.* was voted last winter by the legislature to commence it, and 200 men are already blasting for its foundations. It is eventually to cost 2,000,000*l.* sterling, and fifteen years will be occupied in its construction. This great building is to cover fifteen acres of ground, and is to be situated on Montallan Square, facing Eighth Avenue and Central Park. The front portion is to be finished directly, and the back portion is to be finished from time to time as needed, and as appropriations are made for it. The material is to be granite.

From Nature, **7**, 349, *March 6, 1873.*

Open University and Fourth Television Channel

A FOURTH television channel devoted to education would find favour with the Open University. In the second report of the Vice-Chancellor, published today, Dr Walter Perry says that an education channel which would combine the schools programmes and the further education programmes of the BBC and the IBA with the Open University broadcasts would be "a splendid combination" because the schools programmes and those of the Open University would be broadcast at different times of the day.

Dr Perry said, this week, that there are strong reasons for a fourth television channel for education but that there are enormous political, economic and technical problems to be solved first. But, said Dr Perry, a more practical proposition at present would be the setting up of an educational radio channel.

During 1972, the Open University took up 527 hours of television time compared with about 360 hours devoted to schools TV and 310 hours for further educational programmes on the BBC. The Independent Broadcasting Authority, on the other hand, devotes at least nine hours a week during the school year to school programmes and three hours a week for fifty weeks a year to adult educational programmes. So in all, more than 1,600 hours on all three television channels were devoted to education during 1972.

The Open University calculates that it will need 37 hours a week of television time in 1976—but its present contract with the BBC, which expires in 1976, is for 30 hours. If the university does go on the air for the longer time during the entire university year of 36 weeks, then it will increase the air time from 527 hours to over 1,250 hours.

The total number of hours for education will still, however, be much less than the 6,800 hours a year needed for a full television channel, even if schools and further education programmes are increased drastically.

During 1972 the Open University used up 383 hours of radio time compared with 457 hours for school broadcasts and 354 hours for further education broadcasts. In 1976 the university reckons that it will need more than 1,000 hours of radio time.

But there seems to be little chance of a further television channel being set up before 1976 when the BBC's charter expires and when the independent television companies' contracts run out. A recent question in the House of Com-

mons which inquired whether the Minister of Posts and Telecommunications would authorize the setting up of a second independent television channel was answered with a straight "No" by Sir John Eden. In his report Dr Perry says that the expertise of academics on television has astounded many people and "some old and well-revered shibboleths have been knocked down". In a wider context Dr Perry says that it is more than likely that the educational methods pioneered by the Open University will prove to be of great use "in the larger world outside the university".

As yet, however, the teams making the programmes have not evolved any radically different techniques, but as the teams gain experience of the needs of students such techniques will develop. In particular Dr Perry sees radio vision being used to a greater extent in the future. Radio vision, which is basically

a series of colour slides accompanied by a radio broadcast, is not second best television or glorified radio, says Dr Perry, but a distinct technique with quite definite and specific advantages in its own right.

During 1971 the Open University enrolled 20,000 students at a total direct cost of £2.2 million. The gross income for the year was £7.02 million, of which £6.02 million was granted by the Department of Education and Science, and £0.89 million came from student fees. The remaining £0.11 million was obtained from short-term investments. Sixty-nine per cent of the income was spent on fixed overheads and the remaining £2.2 million on direct student costs. Nearly half the sum spent directly on students went to pay tutors and counsellors—both full and part time, and the remainder was distributed between the cost of home

SELECT COMMITTEE

Hovertrain Demise is Aired Again

THE Select Committee on Science and Technology spent a morning last week trying to nail the blame for its own ignorance of the government's decision to cancel the hovertrain at the door of either British Rail or the National Research Development Corporation (NRDC).

Both organizations knew of the government's decision to cancel Tracked Hovercraft Limited's work when they wrote the memoranda for the Select Committee on the hovertrain in early February. Neither revealed the government's decision, which was not announced until Mr Heseltine gave evidence to the committee on February 14.

The select committee wanted to know why neither body had passed its information on. Mr Richard Marsh, chairman of British Rail, said that it was not BR's job to reveal government decisions. He also pointed out that the select committee had not asked him if the project was to be cancelled. When asked if Mr Heseltine had asked him to keep quiet about the decision, Mr Marsh replied "quite categorically no".

NRDC knew that the decision to cancel would be taken as early as January 23. Its reason for not telling the select committee was that Sir Frank Schon, NRDC's chairman, had made an agreement with Mr Heseltine not to reveal the decision. Sir Frank had been told of the impending decision on

January 23 because an NRDC board meeting on January 24 had to decide whether to proceed with the project. "I insisted that (the decision to scrap the project) was classified information", Sir Frank said.

Mr Richard Marsh, in his evidence, defended the Advanced Passenger Train against allegations made about it last week by the staff association of Tracked Hovercraft Limited. It was not true, he said, that APT had made two unsuccessful runs; it had made one successful one. It is not being significantly rebuilt, as alleged; the gas turbines have been replaced by an electrical propulsion system in the prototype because that had always been planned, not because of problems with the turbines (APTs will be powered by both electric traction and gas turbines when they come into service). The allegations were "totally inaccurate and untrue", Mr Marsh said, "they are wrong, irresponsible and very damaging to our interests".

Mr Marsh emphasized that there was never any competition for government funds between Tracked Hovercraft and British Rail, "at no point have I heard this suggested". But he did say that the cancellation was "one of the few times a government has cancelled (a project) without wasting a great deal of public money". But the parts of the system that had potential had been rescued.

experiment kits, summer schools and printed materials.

The BBC was paid £1.47 million for making programmes which amounted to more than 30 per cent of the fixed overhead expenditure of the university in 1971. At present the Open University programmes are prepared at Alexander Palace, but by 1976 the university hopes that the programmes which it needs will be made at a new audio visual complex to be built on the university campus at Bletchley. The Department of Education and Science has agreed in principle that the complex can be built—to be staffed and manned by the BBC—but at present the university and the DES are negotiating the money to be allocated. This, in the long run, will determine the number of studios to be built, but to build and equip a viable complex will cost about £4 million according to the Open University.

SWINE DISEASE
Control of Swill Plants

A MINISTERIAL order to control the operations of pig swill plants is to be introduced shortly. Fears are growing that unless steps are taken soon the virus that is causing the current epidemic of swine vesicular disease may be recycled through pig swill.

The movement controls imposed last week on pigs throughout England and Wales should do much to limit the spread of the disease—more than 40 out of the 55 cases that have followed the original outbreaks have been attributable to stock movement—but at least five cases may be the result of contam-

Lord Snow to the Fore

SPEAKING at the Annual Dinner of the Institution of Electrical Engineers last week, Lord Snow described plans to shift the balance in universities towards the social sciences as "passing the confines of lunacy".

He went on to say that "we shall be spending thousands of pounds educating young people in social sciences and I cannot imagine any more foolish waste of money". He also bemoaned the fact that engineers in this country are for some reason less respected than in other countries.

Lord Snow said that far from being encouraged to study social sciences, many more undergraduates should be doing hard subjects like mathematics. They could acquaint themselves with social sciences at a later stage, he contended, as people had managed to do quite successfully in the past.

inated swills and the original outbreaks were all on swill-fed farms.

Recycling can occur if a pig is slaughtered while it is incubating the disease (incubation takes 4 to 6 days). Those parts of the animal not used for human consumption go to plants which manufacture pig swill for use on more than 5,000 farms in England and Wales. If the meat from the slaughtered pig is not properly sterilized the virus will be carried over into the swill resulting in further infection.

This may not be the real problem, however. Swill plants are supervised by local authorities, and ministry officials are fairly happy that the meat is being sterilized. The problem chiefly lies in the organization of the plant. Sterilized swill may be recontaminated during the handling of raw swill, and it is this aspect of the operation that ministry officials want tightened up.

Swine vesicular disease is in itself not particularly serious. Infected pigs can recover. The problem is that the symptoms are identical to those of foot and mouth, and if swine vesicular disease was allowed to become endemic in Britain it could mask the much more serious foot and mouth disease. Foot and mouth can kill large numbers of cattle and pigs, and survivors give poor milk and meat yields. The only way to safeguard against this is to stamp out swine disease.

Not that that is proving easy. Although the amounts of virus excreted by infected animals are low compared to the amounts emitted by foot and mouth victims, the swine disease virus is remarkably persistent. There is no question of it being an unbeatable virus, but two of the three farms that were restocked recently have had fresh outbreaks. As a result restocking is not being attempted until eight weeks after disinfection of the farm is complete. Fortunately airborne transfer of the disease is unlikely as the animals excrete only small quantities of virus, and the chief cause of the fifty-five secondary cases has been movement. Twenty herds contracted the disease at markets, five herds were infected by the transfer of infected pigs onto the same farm, and seventeen got the disease from infected lorries. Theoretically lorries are disinfected between each load of livestock, but clearly this is not being done or is not being done efficiently. Greater vigilance and the ban of stock movements should help. Of the remaining cases, one is due to local spread—by vermin or birds—five cannot be easily accounted for, and a further five may be the result of the virus being recycled in swill, although there is no positive evidence that this is so.

Contaminated swill may have been

the cause of the original outbreaks. Poland, Austria, France and Italy all had outbreaks of the disease late last year. Austria almost certainly imported it from Poland. But Poland, France and Italy all import pork from the far east and it is possible that the disease came to Europe that way. Britain too imports pork, although not directly from the east, and it is possible that contaminated carcasses were imported, and their offal used as swill on the five farms were the primary outbreaks occurred.

But whatever the cause, the disease still has to be controlled. The movement ban and swill controls should solve the problem in time, but the persistence of the virus could mean that it will be quite a long time. To date more than 27,000 pigs have been slaughtered, but slaughter seems the only policy. Developing a vaccine to combat the disease would take time, and the rapid turn round on pig farms (the average life of a pig in Britain is a little over five months) would make administering it an almost impossible task.

ISAAC NEWTON TELESCOPE
To Move or Not to Move

THE row over the wisdom, or otherwise, of siting the 98-inch Isaac Newton telescope above the Pevensey marshes of Sussex has surfaced at last in the correspondence columns of The Times. Many astronomers have been unhappy about the location for years, and criticism has reached a high pitch since the inauguration of the telescope five years ago, but for the most part astronomers have succeeded in keeping the debate to themselves. This self-imposed embargo has now been breached by Mr W. Bates of Cheltenham, who wrote to The Times in response to an article by their science correspondent reporting the view of the Director of the Royal Greenwich Observatory, Dr Margaret Burbidge, that the telescope cannot be properly used at its present site, and that ultimately it will have to be moved. "Who," Mr Bates asked, "was responsible for this disgraceful waste of public money? What action is being taken against them?" (The Times, January 31, 1973.)

So far Mr Bates has not had his answer. But Mr P. Lancaster Brown of Beaconsfield, who has written several articles about the telescope, including one commissioned by the Central Office of Information, wrote to give some facts about the history of the telescope (The Times, February 5, 1973). The telescope was first suggested by Professor H. H. Plaskett in 1946 during his presidential address to the Royal Astronomical Society, and the original design was a Schmidt with an aperture

between 49 and 72 inches. The abandonment of this proposal, which some astronomers still regret, came about, according to Mr Lancaster Brown, because some members of the board of management of the project felt that this design would be merely duplicating the Schmidt telescope on Palomar Mountain, California. The telescope that was finally built was a Cassegrain reflector making use of the 98-inch blank presented by the MacGregor Trust of Michigan.

According to Mr Lancaster Brown, the selection of the site was justified on the grounds that the number of clear nights in Britain is not hopelessly inferior to that at the sites of other big telescopes, and he cites the following figures for the number of clear nights per year at Herstmonceux (the site of the Isaac Newton telescope) and two other observatories: Herstmonceux, 1,900 hours; Mount Wilson (California), 2,700 hours; Dominion Observatory (British Columbia), 1,247 hours.

Mr Lancaster Brown says that "in hindsight it seems that the final design choice was mistaken, and that the original Schmidt telescope suggested by Professor Plaskett would have provided a more suitable instrument", but he disputes the view that the construction of the telescope was a disgraceful waste of public money. The question which should really be asked, he suggests, is "Was the meteorological data which influenced the decision to place a large telescope in Sussex wrong"? And he says it would be interesting to compare the number of clear or partially clear nights at the telescope with the number of nights that the instrument has been used by the incumbent staff.

Professor R. A. Lyttleton of St John's College, Cambridge, last week jumped in with a theoretician's view of the debate (The Times, February 24, 1973). He says that the site was chosen for reasons of prestige, even though its unsuitability was known at the time, and that dissenters were warned that any questioning about the site might lead to the cancellation of the project.

Professor Lyttleton goes on to argue that in any case most of the material in the universe is out of sight, so that astronomy is almost wholly a theoretical subject. The money spent on the telescope was enough to set up permanent posts in theoretical astronomy in almost every department of mathematics in Britain.

According to Professor M. J. Seaton of University College, London (The Times, February 27, 1973), Professor Lyttleton's views on the pre-eminence of theoretical astronomy "leads to the most arid scholasticism" (although, to be fair, Professor Lyttleton's letter can also be read as making the point that

observational astronomy should be left to those countries with the right climate). Professor Seaton goes on to say that one of the arguments for siting the telescope in Britain was to give young astronomers an opportunity to learn to use a large telescope, and to develop new techniques of instrumentation. "No one who has studied the problem carefully seriously suggests that the INT should be moved; the decision has been made, the telescope performs a useful function where it is, and the cost of moving it would not be much less than the cost of an entirely new telescope."

Mr Bates, who started the correspondence, would be justified in complaining that none of the letters answers

the points he raised. Professor Seaton notwithstanding, many astronomers would like to see the telescope moved to a more congenial site, and no doubt there will be an interest in the calculations which Professor Seaton says militates against such a move. With there now being talk about the establishment of a new British observatory in the Mediterranean area, possibly on the Spanish island of Tenerife, astronomers will now be wondering whether the arguments which prevented an overseas location for the Isaac Newton telescope will be voiced again. It may well be that at present the greatest obstacle to the establishment of the new observatory is Britain's dispute with Spain over Gibraltar.

INDUSTRIAL INNOVATION

CSII Runs into Hard Times

THE activities of the Centre for the Study of Industrial Innovation have been suspended. Lack of funds and the refusal of British industry to support it have left the centre with little hope of continuing its work except under the wing of a university.

George Teeling-Smith, the centre's director, is "pretty disillusioned about the whole thing". The centre only costs £20,000 a year to run, part of which it earns through contract research, and the simple fact is that industry has refused to help although often paying lip service to the idea.

The centre's financial crisis has been looming for some time (see Nature, 238, 365; 1972). By the end of last year it looked as though the money was not going to materialize and Mr R. Jones, the CSII's resident economist, decided to take a job in industry. The centre aborted its study on the effect of government purchasing on innovation as it was nowhere near finished, and went into hibernation. A few weeks later, but too late in the day, the Social Science Research Council approved a £5,000–£6,000 grant to the centre to study the effects of standardization on innovation.

The centre's best chance of survival lies in cooperating with a university. Both Aston University and the Cranfield Institute of Technology have shown interest. Dr A. H. Chilver, Cranfield's vice-chancellor, said this week that he has discussed the centre's problems with George Teeling-Smith and Edward Hawthorne, one of its trustees, and is eager to define precisely what the centre wants to do and then see if there are ways in which its work could match Cranfield's. "We have no intention of taking the centre over" he said. "We want to see if we can play some part in continuing and developing its work."

If Cranfield does help rescue the centre from its current predicament, funding will almost certainly come from outside the normal run of university sources, possibly from the research foundations. Discussions on finance will take place in the next few weeks. If a link is formed the centre will probably move to Cranfield. "It would probably be important for it to live in an advanced technological environment," Dr Chilver said, "and it would be a logical move to bring it to Cranfield."

Any development resulting from a link with Cranfield would please George Teeling-Smith. "I don't think a relatively small organization will significantly alter the climate for innovation," he says. "British industry needs an atomic bomb under it rather than the squib that we were providing."

Having spent three years being greeted with welcoming smiles but empty handshakes, Teeling-Smith is "a bit sick of the attitude of British industry as a whole". The pharmaceutical companies would have financed the centre (they provided the initial capital), but they already pay for the Office of Health Economics which runs similar studies on health problems, and a similar organization under a different name seemed pointless. The National Economic Development Council (NEDC) contributed, the National Research Development Corporation (NRDC) provided a pittance, and half a dozen other companies stumped up the princely sum of £150 each.

In its three years the centre has published seven reports (one of which for NEDC is due out in March), five of which it researched itself. While its work has not been greeted with total critical approval, it has at least stirred a pot that until recently no one was bothering to watch.

NEW WORLD

Energy from Above and Below

by our Washington Correspondent

FOR many people in the United States, the "energy crisis" finally arrived this winter. Schools and offices have been shut down in several parts of the country because of shortages of oil, and there are now dire warnings of petrol rationing in some areas in the spring. Although there are good reasons to suggest that such acute shortages of oil are chiefly a product of poor distribution and lack of planning and that they are also a direct consequence of the fact that energy is still so cheap in the United States that it is squandered, the energy crisis has triggered a great debate about future supplies and uses of power. Indeed, President Nixon will soon send a message to Congress outlining his Administration's plans for dealing with fuel shortages, and Congress itself is busy forming committees to look into the problems. One result has been an awakening of interest in unconventional sources of energy.

Nobody is suggesting that new sources of energy will help alleviate the present difficulties, but there is hope that they may make a significant contribution to energy supplies by the end of the century. In particular, the Sun and the interior of the Earth are being touted as especially promising sources of power, and two reports prepared with funding from the National Science Foundation have added weight to such suggestions.

As far as energy from the Earth's interior is concerned, one report states that "geothermal resources, by approximately 1985, can have a potentially enormous impact in supplying the nation's need for energy". And the other report, which is concerned with solar power, states that "the panel is confident that solar energy can be developed to meet sizable portions of the nation's future energy needs". The catch, however, is that before such rosy predictions can be realized, large expenditures on research and development will be required, and it seems unlikely that they will be forthcoming.

President Nixon's energy message will undoubtedly highlight the fact that the budget proposes expenditures of $772 million in 1974 on energy research and development—an increase of $130 million over planned expenditure this year. But nuclear energy is set to carry off more than $560 million, with the lion's share going to the breeder reactor, and the total expenditure on solar and geothermal energy together is set for only $16 million. In contrast, the report on geothermal energy recommends expenditures of $41.7 million next year, and the solar energy report calls for $3,500 million to be spent on developing that resource over the next 15 years. The Administration is clearly not quite so enthusiastic.

The chief architect of the report on geothermal energy is Walter J. Hickel, former Secretary of the Interior in the Nixon Administration. With funding from the National Science Foundation's Research Applied to National Needs (RANN) programme, Hickel called together a conference of some 50 scientists and engineers last year, and the report (*Geothermal Energy*, available from the University of Alaska) is the fruit of that conference. Although Hickel is quick to point out that "we do not see geothermal energy as the only answer to the future, nor necessarily the best answer," his report makes the optimistic prediction that geothermal resources in the United States should be capable of supplying some 1,000 million megawatt hours of electricity by 1985 and 3,100 million by the year 2000. In contrast, the power demand of the whole of New England is now less than 60 million megawatt hours a year.

That estimate rests not only on the assumption that a vigorous research and development programme will be funded, but that such a programme will pinpoint and assess geothermal resources in the United States, that it will result in the technology to develop the resources, and that the energy so produced will be able to compete economically with energy produced by other means. The report candidly admits that "only time and research funding can validate or invalidate" those assumptions, but it is pointed out that they have been subjected to the scrutiny of a large number of knowledgeable scientists and engineers, who have concluded that substantial funding is warranted.

The idea of geothermal energy is essentially to tap the great heat reservoir in the Earth's core and to turn it into electric power. The heat, which is derived from radioactivity in the Earth's core and friction resulting from solar and lunar tides as well as the motions of the crustal plates, can theoretically be tapped simply by drilling through the Earth's crust, but it is practical to exploit the heat reservoir only when it is near the surface. And that means chiefly at the edges of the crustal plates and recent volcanic formations. Since much of the western part of the United States has an abundance of volcanic rocks of recent origin, the "potential geothermal resources appear to be very large", the report suggests.

The resources considered for commercial exploitation consist of deposits of superheated steam which contains little or no liquid water, deposits of hot water and hot, dry rocks. Steam deposits are the easiest to exploit since the steam can be fed almost directly into turbines to generate electricity, but they are few and far between. Five such deposits have been discovered, but only three are considered commercially exploitable—one, at Larderello in Italy, has been used to generate electricity since 1904, and another, in Northern California, has recently been exploited.

Deposits of hot water are much more abundant than deposits of dry steam, but they are more difficult to exploit. If hot enough, the water, which is under great pressure in the deposits, could be flashed to steam and used to drive turbines. Deposits of cooler water, below about 200° C, may be exploited by transferring their heat to a more volatile liquid in a heat exchanger, and the vapour from the second liquid would then be used to drive a turbine. This is one area which the report suggests merits further study.

As for hot rock reservoirs, although they are the most abundant geothermal resources, they are also the most difficult to exploit. Several methods have been suggested, all of which involve sinking two holes, fracturing the rock between them with explosives or hydraulically, and circulating a liquid through the fractured hot rock. The report points out that if the technology for recovering the energy from dry rocks is developed, and "once deep drilling technologies are available, geothermal energy sources might be extended to areas of normal heat flow, thereby producing a truly immense energy source".

Hickel's report recommends that the federal government should spend about $680 million over the next ten years on research and development into the exploitation of geothermal resources, nearly half of which should be devoted to resource exploration and development. Other problems needing atten-

tion, the report suggests, are drilling techniques, methods for assessing the size and deliverability of geothermal resources, binary fluid systems for extracting energy from reservoirs which are too cool to provide steam to drive turbines directly, desalination of brines to extract minerals and to provide fresh water along with energy and on the environmental effects of exploiting geothermal power. So far, federal funding on such problems has been small, and there has been a lack of a defined programme for exploiting geothermal energy.

If the report on the potential for geothermal energy is optimistic, the report dealing with solar energy is no less rosy. Prepared by a panel organized jointly by the National Science Foundation and the National Aeronautics and Space Administration, the report concludes not only that "there are no technical barriers to wide application of solar energy to meet US needs", but also that a "substantial development program" could meet the necessary technical objectives by the year 2020. By that date, the panel believes that solar energy could provide economically up to 35 per cent of total building cooling and heating, 30 per cent of gaseous fuel used in the US, 10 per cent of the liquid fuel and 20 per cent of the electric energy requirements.

All that is needed for solar energy to live up to these predictions is a research and development budget of some $3,520 million over the next 15 years, some technological breakthroughs and the work of market forces which are expected to increase the cost of energy from other sources to make solar power more competitive. In short, the panel suggests that "on close examination, the possibilities for the economic use of solar power, given reasonable R and D support, appear much better than generally realized".

The research and development programme outlined by the panel would concentrate on three chief areas of direct use of solar power—thermal energy for buildings, the production of fuel from organic materials and electric power generation by thermal conversion and by photovoltaic cells—and in addition the panel suggests that wind energy and thermal differences in the oceans could be tapped for electric power generation. Major technical problems remain to be solved in each area, but if the funding is made available, the panel believes that solar power could be used to heat buildings in about 5 years' time and cool them in about 6–10 years, that synthetic fuels could be produced from organic materials in 5–8 years and electricity in 10–15 years.

Residential heating and cooling "has the highest possibility of success", the

panel suggests, but there is need for development of more efficient solar heat collectors for use on rooftops, and the efficiency of cooling systems powered by solar heat must be improved. Nevertheless, the costs of developing such a system are reckoned to be about $100 million over 15 years, which is a small fraction of the predicted fuel savings.

One reason why both geothermal power and solar energy are receiving considerable attention in the United States is because they have the backing of environmentalist groups. The energy crisis seems likely to hurt the cause of environmentalists badly, particularly if they are blamed for part of the shortages by blocking nuclear power plants or the Alaska pipeline, and environmentalists are urging research and development on those forms of energy production which are likely to have the least impact on ecological systems.

Solar energy seems to fit that bill, since for applications such as building heating and cooling and electric power generation, little or no waste products are formed, and no resources would be depleted. Geothermal power production, on the other hand, is likely to involve noisy, dirty plants, and there is possible environmental damage from contamination of groundwaters with brines that are reinjected into the soil. Nevertheless, the environmental damage from such power plants would be

limited exclusively to the site, since they would use no transported fuel, nor require the disposal of radioactive or other toxic wastes.

Whether the hopes of the environmentalists or the rosy predictions of the two reports on solar and geothermal energy will be realized seem to depend chiefly on research funding and the solution of important engineering problems. The Administration is, however, understandably sinking its money into less technologically uncertain ventures, such as the breeder reactor.

BIOMEDICAL RESEARCH

Medical Ethics Examined

by our Washington Correspondent

THE Senate Health Subcommittee last week held three days of hearings on biomedical research involving human subjects, and it opened up a Pandora's Box of problems involving medical ethics. The hearings ranged over cases of unapproved contraceptive drugs being given to poor people in Tennessee and to university students in the United States, and they also took a look at some of the medical issues involved in the fields of brain research and psychosurgery.

Few questions were answered—that was not the object of the exercise—but with good stage management, human interest, pathos, displays of anger and, of course, the drawing power of

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ASTRONOMY

Funds for Poland from the NSF

by our Washington Correspondent

THE National Science Foundation has announced that it will release $1.4 million in Polish currency owned by the United States for construction of a centre for theoretical studies in astrophysics. The centre, which will be built in Warsaw, has been under consideration since 1971, and the announcement of the plans coincides neatly with the current celebrations of the 500th anniversary of the birth of Copernicus.

The money will be spent over three years, as part of the NSF's Special Foreign Currency programme, which uses currency derived chiefly from the sale of agricultural products for scientific purposes. The Polish Academy of Sciences will also put up about $622,000 for furnishing and equipping the centre, and will support its operation. Poland is one of eight countries which benefits from the special currency programme.

The astrophysical centre will consist of laboratories, a lecture room, a computing centre, administrative offices and facilities for visiting scientists, housed in a building with some 56,000 square feet of floorspace. Construction is due to begin in June, and the building should be ready by October, 1975. It will be named the Copernicus Astronomical Center.

In November last year, the governments of the United States and Poland signed a broad agreement on cooperation in science and technology, which included plans for sharing of research data between scientists in the two countries and the exchange of personnel. Although the Copernicus Astronomical Center was being planned well before the agreement was reached, it is the first large project to be announced since the agreement was concluded last year.

Senator Edward Kennedy, the chairman of the subcommittee, they received considerable public attention. The central issue to emerge from the hearings is simply how can the rights of a patient be best protected, without undue interference from the Federal government in the practice of medicine?

The first two days of hearings centred on an apparent loophole in the food and drug laws which allows drugs to be prescribed, sometimes on a large scale, for unapproved uses. When a new drug is placed on clinical trials, the Food and Drug Administration requires an investigator to obtain a permit, his trials are closely monitored, and several precautions are required to ensure that the patient is aware of the risks involved in the trial. The same procedure must also be followed when a drug which has already been approved for one use is tested for a different application, but since that drug will already be in the pharmacies, there is nothing to prevent a doctor prescribing it to a patient for the unapproved use. In such a case, there is no legal requirement for ensuring that the patient is in fact, fully informed of the risks involved.

"The prescribing of an approved drug for an unapproved use by individual physicians in the practice of medicine is beyond the jurisdiction of the FDA," Dr Charles C. Edwards, Commissioner of the agency told the Kennedy subcommittee last week. He pointed out that the history of the Food and Drug Act is replete with statements that Congress does not intend the FDA to regulate the practice of medicine between the physician and his patients.

"We cannot, in good conscience, require that a physician watch a patient's condition worsen because the package insert provides for only a low dose of the drug or contains an applicable warning or contraindication," he said. And nobody who spoke at the hearings disagreed.

But what concerned Kennedy was reports that two drugs, Depo-Provera, a progesterone derivative, and diethylstilbestrol, which are approved for a variety of uses but which are supposed to be on clinical trials as birth control agents, are being prescribed in large quantities, and it seems, without sufficient safeguards to protect the rights of the recipients.

Depo-Provera has been marketed for several years for the treatment of inoperable, recurrent uterine cancer, and it has also been under clinical trials in the United States as a birth control agent since 1963. Its promise as a birth control drug lies in the fact that it needs to be administered only once every three months, by injection, and it seems to be highly effective. But in 1970

studies in dogs revealed that Depo-Provera produced mammary tumours, and according to Dr Edwards, an FDA advisory committee believes that long-term metabolic studies are still required before the drug can be approved as a contraceptive agent. Its use is, in any case, intended only for those who have tried all other birth control methods without success. In 1970 there were about 1,000 patients involved in FDA trials of the drug, but the number has now dropped to about 140.

But health officials in the state of Tennessee are not prepared to wait for the FDA to approve the drug before making it available through state-run family planning clinics. Dr Robert H. Hutcheson Jun., Assistant Commissioner in the Tennessee Department of Health, told the committee that 942 patients in Tennessee are receiving Depo-Provera from family planning programmes, and Dr James Brown, superintendent of a mental institution near Memphis later testified that the drug is administered to 181 women in his hospital to prevent pregnancy and to prevent menstruation for hygienic reasons.

Dr Hutcheson further testified that although they have the same information as the FDA, health authorities in Tennessee came to a different conclusion from the federal agency, believing that the drug is safe for use in some cases. The result is that there are now nearly ten times as many patients receiving Depo-Provera for birth control in Tennessee than are receiving it through the FDA monitored clinical trials.

A critical issue is whether the patients treated in Tennessee are informed of all the risks involved in the treatment before they give their consent. Hutcheson pointed out that they all sign a form detailing the risks, but Kennedy pointed out that the form is not as detailed as the consent forms drawn up by the FDA for their clinical trials of Depo-Provera, and Marsha Greenberger, an attorney for the Center for Law and Social Policy, provided documentation to the committee to back up her assertion that at least six patients were completely unaware of the risks.

Depo-Provera is marketed solely by the Upjohn Company, and it is thus relatively easy to control from the source. Dr W. N. Hubbard Jun., executive vice president of the company, told the Kennedy committee last week that his company has already stopped shipments to the Tennessee health department. He also said that sufficient evidence has been accumulated to make a decision on most questions surrounding the drug, and there is therefore no reason for the FDA to issue an investigatory permit to the

Tennessee health department—such action would not contribute to clinical evaluation of the drug.

As for diethylstilbestrol (DES), the committee received evidence that it is being dispensed quite freely from some university health services to prevent pregnancy after intercourse. DES is approved by the FDA for several gynaecological disorders, but it has been found to be associated with cancer of the vagina in young women whose mothers had taken the drug during pregnancy. The drug has also been found to be a potent post-coital contraceptive agent, and since it is readily available in pharmacies for its approved uses, the drug has been widely prescribed to prevent pregnancy.

Dr Edwards acknowledged last week that such prescribing is taking place, and he also announced that the FDA is about to approve DES as a post-coital contraceptive in emergency cases only—after rape or incest. He added that if pregnancy does result, even after taking DES, the patient should seriously consider abortion. The announcement immediately drew protests that it would make prescribing of DES even more widespread, and that since it now carries FDA approval—albeit a very restricted approval—many women will not consider the risks involved very seriously.

Dr Edwards said in his testimony that in all cases of drug investigations on humans, the ultimate responsibility for advising patients of the risks involved, and for following up on the treatment rests with the investigator. He added that better prescribing of drugs may be brought about by continuing education of doctors, and by better peer review mechanisms. Those suggestions were generally accepted by other witnesses before the committee, and it was also generally agreed that informed consent is the central requirement in any investigational procedure.

Surprisingly, however, the case of methadone, which embodies many of the questions raised during the hearings, was not brought up in the discussions. While the drug was on trial, the FDA allowed its use to mushroom by issuing many more investigationary permits than needed just for clinical information.

Then, when the FDA approved methadone for use in the treatment of heroin addiction, it withdrew the drug from pharmacies and stipulated that it would be made available to drug clinics directly from the manufacturers, thereby depriving other doctors of the ability to prescribe an approved drug. In that case, the FDA clearly regulated the practice of medicine between the physician and his patient. Considerations of practicality aside, such actions raise a number of difficult questions.

NEWS AND VIEWS

Studying the Formation of Ocean Floors

EVERY year some 10 km³ of molten rock are transferred from the mantle into the crust of the Earth. The eruption south of Iceland, which began on January 23 and was heralded by the opening of a fissure 1.5 km long, typifies this process. Indeed most of this igneous activity occurs along the ocean ridges from which the newly formed rocks move outwards at a few centimetres a year to form the ocean floors. Although this is undoubtedly the most important rock-forming process in the outer part of the Earth and the localities where it occurs are very precisely known, it remains a remarkably difficult pheno-menon to study. The difficulty arises from the high density of the rocks involved, for these mafic and ultra-mafic rocks are so heavy that they are rarely uplifted to be exposed by erosion.

The problem has been attacked in three ways; by observations in the field, notably in Iceland where part of a mid-oceanic ridge lies above sea level, by geo-physical studies of the deep ocean floor, supplemented by drilling and by examination of material recovered from submarine fault scarps, and by investigation of the handful of places where fragments of seafloor have been uplifted in regions where the oceanic crust has been trapped between two advancing continents. All three lines of attack produce an idealized model of an oceanic crust a few kilometres thick, having at its base mantle rocks from which the overlying igneous rocks have been derived. Above this depleted mantle follow mafic intru-sions, partly gabbroic but characteristically in the form of numerous vertical dolerite dykes; at some levels these are so numerous that no other rock is present. Most of these intrusions, which collectively form an irregular layer, apparently had no connexion with the surface, but some fed an overlying succession of lavas which constitute the uppermost storey of this igneous succession. The accumulation of sedimentary rocks as this igneous sequence ages and is carried away from the ocean ridge where it originated completes a horizontally layered sequence of a kind which seems to underlie all the principal oceans.

The well-known magnetic anomalies seem to originate in the uppermost parts of this succession, implying that some process has greatly reduced the remanent magnetism of the lower parts. The recovery of metamorphosed rocks from the ocean floor and from submarine scarps has led to the suggestion that widespread metamorphism might be the cause of such changes. As Van Andel has expressed it, such a regional metamorphic layer would place a floor under the zone responsible for the observed geomagnetic anomaly patterns.

The Troodos mountains in Cyprus were first identified as a possible upthrust slice of oceanic crust and mantle by Gass and Masson-Smith in 1963. On page 26 of this issue of *Nature* Gass and Smewing further develop this hypothesis and in particular describe the work they have carried out from the Open University on the zeolites and their distribution throughout the Troodos massif. The new evidence provides further indications of how the Cyprus rocks can, in conjunction with the volcanic suc-cessions developed in Iceland, be employed to give what is probably the most complete model deduced from ex-posed rock or an ocean ridge in cross-section. With the aid of such a model one can tackle two problems: How did the rocks form in the first place? What modifica-tions are likely to have occurred subsequently? A critical part is played by the vertical dykes which at depth make up the whole Troodos complex in Cyprus, and in Ice-land, where higher sections are exposed, increase in number downwards through the volcanic succession. The discovery of this remarkable structure, essentially a pile of volcanic rock underlain by ever increasing num-bers of dolerite dykes, was made almost simultaneously by Wilson in Cyprus and by Walker in Iceland. Both appreciated the significance of what they had found, and realized that the presence of vertical dykes indicated a considerable extension of the crust. Walker postulated a 400 km extension below Iceland, and Wilson commented "the sialic crust appears to have moved away under great tensional stress while the numerous dykes were extruded". Such interpretations, made in the late 1950s before Hess's statement on seafloor spreading, were remarkably pre-scient comments.

Gass and Smewing record the metamorphic changes they have observed in Troodos. The zeolite zones they recognize correspond to the deeper zones identified in Iceland. In Cyprus these pass downwards into green schist rocks metamorphosed at still higher temperatures. The nature of the igneous rocks of the Troodos Complex has already suggested that a deeper section through old oceanic crust is exposed than is found in the Tertiary rocks of Iceland. The new evidence on the metamorphism in Cyprus confirms this relationship. Among the interest-ing matters that Gass and Smewing have established is the fact that an early series of volcanic rocks had been metamorphosed and then eroded in part before a later series of pillow lavas accumulated.

A general point that Gass and Smewing develop is the possibility that physical changes produced by meta-morphism may account at least in part for some of the layered structure which characterizes ocean floors. In this they are following up earlier work in the Atlantic and on Iceland, where, for example, Gibson and Piper showed that increases in density produced by the devel-opment of zeolites in volcanic rocks could account for the properties of layers 1 and 2 indicated by seismic studies below Iceland.

Crust is formed at a spreading ridge in two different though closely related fashions. The vertical dolerite dykes, arranged like a pack of cards on edge, increase in number as movement continues and so build up a

layer, possibly layer 3 of the ocean floor. The over-lying layers 1 and 2 seem to be constructed partly of dykes and partly of lava flows, the proportion changing as one goes upwards through the crust. In Iceland, where such lavas have been most closely studied, they are stacked like shingles on a roof dipping inwards at 5 to 10° towards the centre of the island. It is not at all easy to attach individual flows to the dykes that supplied them. Fortunately, very distinctive features are present, which enable one to learn something of the way in which the volcanic rocks develop. At local centres within the Icelandic lavas an unusual variety of magmas are erupted; the resulting lavas include acid rocks, readily identified among the predominantly basaltic pile; their distinctive nature and the way in which they increase in thickness toward the centre from which they were erupted make it possible to identify several central volcanoes.

The work of Icelandic and British geologists has shown how these centres remain active for about a million years during which time they must be transported many kilometres outwards from the spreading axis. In most instances they then become extinct and their place is taken by a new volcanic centre formed near the ridge, which in turn is displaced for a few tens of kilometres, erupting volcanic rocks as it goes. In this way, as Gibson and Piper (*Phil. Trans. Roy. Soc. Lond.*, **A271**; 1972) have shown, successive groups of lavas, each with its attendant central volcano, come into being and are transported outwards and overlapped by younger lens-like units of lava flows. J. S.

Bacterial Polarity

THE central feature in theories of how genes are controlled, both in bacteria and in the cells of higher organisms, almost always consists of a model to explain how their transcription into messenger RNA is induced or repressed. But in spite of the considerable progress which has been made in tracing formal control networks and defining their biochemistry, details of the enzymatic processes by which RNA chains are initiated, elongated and terminated have remained elusive. De Crombrugghe and his colleagues at the National Institutes of Health, in their earlier articles, concentrated their attention upon the control of bacterial operons at the initiation of transcription (see *Nature New Biology*, **231**, 139; 1971). They now report, in last Wednesday's issue of *Nature New Biology*, **241**, 260; 1973), that they have extended their studies to the termination of transcription, which may provide a hitherto unsuspected control of gene expression in bacteria.

Initiation of transcription usually seems to be the crucial step in controlling gene activity. Initiation in general depends on one polypeptide component of the bacterial RNA polymerase, the sigma factor. In many bacterial operons, however, an additional control protein—which is activated by cyclic AMP—must be present to assist the initiation of RNA synthesis. This interaction, coupled with the inhibition of transcription by repressor proteins, accounts for the control of expression of inducible and repressible operons. Uninfected bacterial cells contain only one sigma factor, but when phage DNAs infect a

host cell they may cause the replacement of the sigma factor of the host polymerase by a phage-coded protein which changes the specificity of transcription.

Termination of transcription has more recently begun to seem a plausible mechanism for controlling gene expression during phage infection; it now seems almost certain that one of the first products specified by an infecting phage DNA is an anti-terminator protein which allows the host polymerase to "read through" sites at which it would otherwise terminate on the phage genome. The bewildering multitude of sigma factors seems to have been an artefact, for the introduction of changes in the initiation machinery of the host takes place only at a later stage.

Termination is catalysed by one of the innumerable protein factors of macromolecular metabolism in bacteria, the rho factor. Since the discovery in bacterial cells of this component which acts as a template of phage DNA (and which is antagonized by the anti-terminator proteins synthesized during infection), the involvement of this protein in RNA synthesis in the host bacterium has been a considerable puzzle. De Crombrugghe *et al.* now provide the first demonstration that rho factor is active with bacterial DNA.

The three genes of the galactose system of *Escherichia coli* are transcribed in the order *galE-T-K* both *in vivo* and *in vitro* when they are part of a phage lambda DNA molecule. When RNA polymerase is allowed to transcribe this template in the absence of rho factor, very large molecules of RNA are synthesized, presumably because the enzyme reads past the end of the galactose operon into the regions of phage DNA. When a low concentration of rho is added, however, the largest RNA molecules sediment at about 22–25S, which corresponds to the size of the transcript expected from the complete *gal* gene cluster; the smallest RNA molecule in this gradient sediments at about 12–15S, which is about the size expected of a transcript of the first gene, *galE*, alone. Hybridization experiments in which the RNA product is annealed to denatured DNAs derived from phage genomes which carry only part of the galactose operon confirm the idea that the large molecules of RNA correspond to *galETK* and the small ones to *galE* alone. This suggests that low concentrations of rho cause some polymerase molecules to terminate transcription at the end of the *galE* gene, although others continue past this site to a second termination sequence located at the end of the operon. When the concentration of rho is increased, all the polymerases terminate at the first site, for the sole product of the reaction is an RNA of about 14S corresponding to *galE* alone.

The traditional view of transcription of bacterial operons is, of course, that they are synthesized into long polycistronic mRNAs—which represent the sequences of all the genes of the operon. These messengers are sequentially translated into the various proteins for which they code. Termination of transcription within an operon is not succeeded by reinitiation and synthesis of a messenger for the remaining genes, for De Crombrugghe *et al.* find no transcripts corresponding to *galTK*. If conditions *in vitro* reflect those which prevail *in vivo*, internal termination may cause the production of more messenger sequences for early genes in the operon, leading to increased synthesis of their protein products relative to the later genes. On the other hand, the presence

of internal termination sites may reflect the evolution of gene clusters from independent genes and they may be ignored by the rho factor in the conditions prevailing *in vivo*.

An important difference between the conditions of transcription *in vitro* and *in vivo* is that translation proceeds simultaneously with transcription in the cell, but the messengers are not translated *in vitro*. One consequence of the failure of simultaneous transcription and translation in the cell is polarity ; mutants which cause termination of protein synthesis in one gene change the properties of messenger RNA representing subsequent genes. Two theories have been proposed to explain this polarity. One explanation is that messenger is synthesized beyond the mutant site but is degraded by cellular nucleases because it is no longer being translated ; the other postulates that translation is needed if transcription is to continue so that the enzyme ceases RNA synthesis at or soon beyond the mutant site (see *Nature New Biology*, **232**, 161 ; 1971).

Polarity can be caused by the presence of nonsense mutations and by the insertion of foreign DNA into the operon. Insertion mutants differ from nonsense mutants in that they are always extremely polar and their polarity does not show the dependence on position within the gene characteristic of nonsense mutations. De Crombrugghe *et al.* have found that one such insertion mutant where the insertion is located close to the beginning of the galactose genes is transcribed normally *in vitro* by RNA polymerase. But if rho factor is added to the incubation, transcription terminates within the inserted sequence. The insertion is very sensitive to rho and reacts at even the lowest concentrations of the factor.

In this situation, polarity results from rho-dependent termination. Does a similar mechanism explain the polarity of nonsense mutations, perhaps, for example, because nonsense codons constitute part of the DNA sequence recognized by rho factor? Polar nonsense mutants in the galactose operon proved to have no effect on transcription, however, in either the absence or presence of rho. This implies that the polarity of nonsense mutants depends on the failure of translation as such and not on the sequence of the nonsense codons themselves.

How widespread is the use of rho in bacterial operons? At least one other operon, the lactose operon, contains rho-sensitive signals, for De Crombrugghe *et al.* find that low concentrations of rho seem to cause transcription to halt at the end of the operon ; but high concentrations generate a small RNA product, sedimenting at about 12–14S, which is of the size expected to correspond to only the first one-third or so of the *z* gene, the first gene of the operon. The correspondence of this location with a peak in the gradient of polarity (a region in which polar mutants have less effect upon the expression of subsequent genes) suggests that termination does not result from rho action at a site which by chance resembles true terminator sequences ; it seems likely that the action of rho *in vitro* reflects the organization of the *z* gene *in vivo*. One possible implication is that the *z* gene may in fact comprise two genes, not one as has previously been thought.

The immediate significance of rho-dependent termination within an operon is that this mechanism may explain the natural polarity of some operons, in which later genes direct synthesis of less protein than earlier genes. This

might be achieved by utilizing signals at the ends of genes which have lower affinities for rho than those at the ends of genes; rho recognition signals may yet prove to be present at the ends of all genes in an operon. Another variation on this theme is to suppose that there might be different kinds of rho factor to recognize the different signals. Conditions in the cell may differ appreciably from those *in vivo* so that defining the function of the rho factor as a cellular control protein must demand the isolation of mutants in the termination protein. De Crombrugghe *et al.* say that their next experiments will be to test the intriguing speculation that rho-dependent termination may provide an alternative explanation for the polarity of nonsense mutants ; perhaps internal rho-dependent termination sites are activated when translation ceases at a previous nonsense mutation.   B. L..

Cell Cycle in *Xenopus*

BETWEEN the stages of early gastrula and late neurula profound changes take place in the *Xenopus* embryo ; the cells undergo about three divisions, increasing seven to eight times in number, and differentiated tissues such as notochord, neural tube, muscle somites and gut become recognizable histologically. But what would happen, one may ask, if mitosis is inhibited at the early gastrula stage, so that there can be no increase in cell number? The results of this intriguing experiment are reported on page 55 of this issue of *Nature* by Jonathan Cooke, of the University of Sussex.

Rather surprisingly Cooke found that nothing very drastic does happen to the development of the embryo if cell division is totally and rapidly inhibited at the early gastrula stage, either with colcemid or mitomycin C. The late neurula has all the differentiated tissues and morphology of the normal embryo, but only about one eighth the number of cells, which are correspondingly larger.

By itself this result is interesting in that it suggests that cells in the embryo do not have to go through a fixed number of divisions or normal chromosomal replications before differentiating. It does not, however, exclude the possibility that cells have to traverse part of the normal cell cycle to be able to respond to a change in positional information, a suggestion which has come from work on the insect cuticle. To test this hypothesis, Cooke transplanted a dorsal lip organizer into an inhibited embryo. This operation resulted in a second site of ectodermal invagination and the development of a second neural tube and notochord. In this way host cells were committed to a completely different developmental fate even though they could not undergo cell division. Experiments are in progress to test whether DNA synthesis and abnormal chromosome replication are still taking place in the colcemid-inhibited cells, and whether these processes are absolutely required for morphogenesis and differentiation.

From a Correspondent

VISION

Visual Feedback

from our Animal Behaviour Correspondent

AN ingenious series of experiments carried out on kittens during the past 10 years at the Massachusetts Institute of Technology establishing the conditions necessary for the development of normal visual-motor coordination have shown that kittens require visual feedback from the result of their own movements. Kittens moved passively through the environment without experiencing the visual consequences of moving their limbs remain ill coordinated, unable to direct their movements and apparently with little idea of the spatial configurations of the environment.

In the latest of this series of studies, A. Hein and R. M. Diamond (*J. Comp. Physiol. Psychol.*, **81**, 394 ; 1972) have attempted to separate two components of this visual feedback: "seeing arm limb movements" and "seeing environment change as result of own movement". Their results suggest that it is not sufficient for a kitten to see its limbs move in isolation from the rest of the environment ; only if the kitten has also experienced some other aspects of its visual environment in relation to its own movements will it be able to perform such tasks as reaching out a paw and touching a bar.

Hein and Diamond gave kittens experience of visual feedback from their paws in isolation from other sorts of visual experience by putting a spot of luminous paint on one paw and keeping the kittens in the dark. In this way, the only thing they could see was a patch of light as their own paw moved. Perhaps not surprisingly, after 10 days of this, the kittens gave evidence of being very ill coordinated, unable to reach out towards objects, and bumping into obstacles. They were then allowed experience of a normally illuminated room. Half of them had opaque collars on so that, although they could move freely about, they could not see their own limbs and so did not receive visual feedback from their own limb movements. The other half were not only prevented from seeing their own limbs but were restrained in a holder, so that they could only see what was going on around them. After 10 days of this treatment, none of the kittens showed visually guided reaching—that is, when they were lowered towards a ladder, they did not reach out their paws towards the rungs. But the kittens that had been allowed to move freely were superior in one respect: they avoided obstacles when moving around, unlike the restrained kittens. All kittens were then given a further 10 days of the luminous paw

treatment, but this time the spot of paint was put onto the opposite paw from that in their initial exposure. As before, the only thing the kittens could see during this time was the spot of paint on their paw, as the rest of their environment was in total darkness.

It was after this treatment that the difference in reaching ability between restrained and unrestrained kittens became apparent. Only the animals that had previously developed visually guided locomotion (the ability to avoid obstacles by visual means, for example) showed properly developed visually guided reaching. What was even more remarkable was that they could reach correctly only with the paw which had had the spot of paint on it and from which they had had visual feedback, in the third part of the experiment. They were unable to guide their other paw correctly. Kittens which had been restrained and had never developed the ability to move around without bumping into things could not reach correctly with either of their paws.

Previous studies had shown that in the kitten, visual feedback from a moving limb is essential for the development of properly coordinated visually guided reaching. This experiment has added a proviso: it would seem that visual feedback from the forelimb is sufficient for the acquisition of visually guided reaching only if visually guided locomotion around the environment has also been developed.

PROTEINS

Hunting the Hybrid

from our Molecular Biology Correspondent

ONE of the unswept corners of haemoglobin chemistry, which has irked the practitioners for some time, is the balance of species present in a mixture of two haemoglobins, such as occurs in sickle-cell trait blood. Electrophoretically, normal adult and sickle-cell haemoglobins, $\alpha_2^A \beta_2^A$ and $\alpha_2^A \beta_2^S$, separate easily enough, but because the haemoglobin tetramer is in rapid equilibrium with its symmetrical $\alpha\beta$ dimer, there should be every reason to expect the hybrid $\alpha_2^A \beta^A \beta^S$ to be represented in the mixture. This, however, is an elusive creature, which escapes its pursuers by dissociating during the fractionation process: the hybrid will have an electrophoretic mobility between those of the parent species, haemoglobins A and S. The dimers $\alpha^A \beta^A$ and $\alpha^A \beta^S$, in equilibrium with the hybrid tetramer (no matter in how low proportion), will accordingly separate from the latter, one ahead and one behind, and turn respectively into $\alpha_2^A \beta_2^A$ and $\alpha_2^A \beta_2^S$ tetramers. Unless then the dissociation to dimers can be inhibited, the existence of the hybrid, like the extinguished light in the refrigerator when the door is shut, can only be taken on faith. Macleod and Hill (*J. Biol. Chem.*, **248**, 100 ; 1973) have now finally found a method, using a covalent cross-linking reagent, to salt the beast's tail.

Oncogenic Potential of *Herpesvirus saimiri*

Herpesvirus saimiri, which is indigenous to squirrel monkeys and which has not been associated with any disease, malignant or otherwise, in animals of this species, has of late attracted the attention of tumour virologists because when it is inoculated into other primates—marmosets, ringtail, owl and African green monkeys, for example—it induces lymphomas or leukaemias. Virtually nothing is known to date about the molecular biology of this oncogenic herpesvirus, but as Ablashi and seven colleagues report in *Nature New Biology* next Wednesday (March 7), the oncogenic potential of this virus remains after the virus has been heat inactivated such that it can no longer replicate and kill owl, monkey and African green monkey cells.

Ablashi *et al.* propagated and isolated infectious *Herpesvirus saimiri* in Vero cells, a stable line of cells derived from African green monkey tissue. They then inactivated the viral particles by heating them to 56° C for 30 min. Intact viral particles were not morphologically changed by this treatment

although the capsids of unenveloped particles appeared to collapse during heating. After this treatment the virus failed to produce any cytopathic effect in Vero cells or in owl monkey cells. Four owl monkeys, however, after receiving six weekly injections of the inactivated virus, eventually developed malignant lymphomas the pathology of which is described in some detail by Ablashi and his colleagues. Furthermore, infectious *Herpesvirus saimiri* could be recovered, by co-cultivating, with Vero cells or owl monkey cells, tissues collected from the lymphomatous owl monkeys at necropsy.

It seems, therefore, that *Herpesvirus saimiri* inactivated by heat so that it is no longer able to kill susceptible host cells may retain not only the ability to transform cells and induce tumours but also retain the genetic information required to code for complete infectious progeny viral particles. The precise nature of the molecular mechanisms that underlie these phenomena remains unknown, but it seems clear that the cytocidal and oncogenic potential of this virus can be separated.

Internal cross-links were introduced in the tetramers of a haemoglobin A and S mixture with a bifunctional fluorodinitrobenzene, specifically *p,p'*-difluoro - *m,m'* - dinitrodiphenylsulphone. Gel electrophoresis after reaction revealed a third component, running between the A and S zones. This is not, of course, proof of the presence of a hybrid, for the annihilation of amino groups—actually as shown in earlier work, the α-chain termini — by the cross-linking reagent renders any identification based solely on electrophoretic mobility uncertain. Macleod and Hill therefore went on to isolate the hybrid in the following way: concentrated magnesium chloride was added to the mixture after reaction, so as to dissociate all dissociable haemoglobins into αβ dimers. Any molecules cross-linked across their α or their β chains are unable to dissociate, and this fraction, which seems to be rather more than half of the total in the conditions used, is collected by gel filtration. Ion-exchange chromatography of this material gives rise to three principal fractions. By contrast the undissociable fraction in haemoglobins A and S mixed after separate exposure to the cross-linking agent generates only two components, corresponding to the first and the third species eluting from the heterologous system. The inference is that the middle peak is the cross-linked hybrid, $\alpha_2^A \beta^A \beta^S$, and it is shown to be such by analysis of the product of trypsin hydrolysis, in which the characteristic β^A and β^S peptides are present in equal amount.

The concentration of the cross-linked hybrid formed in an equimolar mixture of haemoglobins A and S is actually considerably greater than that of either of the homologous hybrids, and it therefore seems that the hybrid tetramer is not merely a significant, but in fact the preponderant, component in sickle-cell trait haemoglobin at equilibrium. This gives substance to a suggestion concerning the low probability of sickling in erythrocytes of sickle-cell heterozygotes, compared with homozygotes. It has been conjectured that the polymerization of the haemoglobin S in the cell is impeded by the incorporation of hybrid tetramers into the aggregates.

A different use for bifunctional reagents is as a means of restricting structural adjustments between the haemoglobin subunits during the oxygenation process. Cross-links within the β chains have been found sufficient to inhibit the transition to the low-affinity state. An interesting new essay in this direction comes from Fasold, Meyer and Steinkopff (*Europ. J. Biochem.*, **32**, 63 ; 1973), who have used a reagent based on iodoacetamide, with the built-in advantage that it can be cleaved in the middle by reduction of an azo link. The reagent is *p*-bis-iodo-acetamide-2,2'-dicarboxyazobenzene; it is rigid, and can therefore only join reactive groups separated by a prescribed distance with rather little tolerance. Rapid reaction occurs with haemoglobin, with uptake of two moles of reagent per tetramer, after which a slower reaction supervenes.

The product of the first reaction, when fractionated on an ion-exchange column, contains one major component, which is tetramic, and possesses two α and two β chains, with one cross-link per β chain, for in a hydrolysate two groups in either are found to be carboxymethylated. The cross-link, which joins cys-93 to lys-82, is submerged in the molecule, more or less under the F helix. A minor product of the reaction also contains two cross-links, which, however, are asymmetrically disposed, one lying within a β chain, as in the major product, the other linking the cys-93 of the second β chain to his-45 of the neighbouring α chain. The corresponding monofunctional reagent blocked only the cys-93 of each β chain. The introduction of this foreign body into the vitals of the haemoglobin molecule caused a diminution in the haem-haem interaction, with a drop in the Hill constant to 1.7. With cross-links in the β chains, on the other hand, the Hill constant dropped to unity, and the same was found for the asymmetrically reacted species, in which only one β chain contains a cross-link. The authors suggest that the transition between the high and low-affinity conformational states may be repressed with some degree of independence at

DNA Synthesis in Developing Sea Urchins

IN next Wednesday's *Nature New Biology* (March 7), Infante and his colleagues report the isolation from the nuclei of developing sea urchin embryos of a DNA-membrane complex which supports DNA synthesis both *in vivo* and *in vitro*. The natural synchrony of the first few cellular divisions after fertilization of the sea urchin egg facilitates study of the different stages of the division cycle.

Nuclei were isolated from embryos containing completely labelled DNA. The nuclei were lysed with detergent and the lysate was centrifuged on a discontinuous 15–40 per cent sucrose gradient. The bulk of the DNA was found free at the top of the gradient, but 10–30 per cent formed a band (the M-band) at the 40 per cent sucrose layer and was associated with membrane material. Treatment of the M-band complex with DNase, RNase, pronase, phospholipase-C and deoxycholate indicated that DNA, RNA, protein and phospholipids were all important in maintaining the integrity of the M-band.

When embryos in S-phase were pulse labelled with ³H-thymidine for 30 s at 17° C, more than 70 per cent of the labelled DNA was located in the M-band. The remaining labelled DNA, located in the top fraction of the gradient, was demonstrated to be released DNA originating in the M-band when the labelling experiment was repeated at 5° C, at which temperature DNA synthesis is greatly retarded. At 5° C, all the DNA synthesized in a 30 s pulse was localized in the M-band. Although, following an extended labelling period of 10 min, the bulk of the DNA was found in the top fraction of the gradient, all of the DNA made in a 330 s pulse at the end of this 10 min period was located in the M-band. Thus DNA replication seems to occur at the membrane and non-replicating DNA is located in a fraction which is more readily dissociated from the membrane complex.

Further experiments, in which embryos were labelled for 35 min starting in the S-phase and ending in G2, showed that, as the cells entered G2, virtually no DNA could be found associated with the M-band. Thus the formation of the DNA-membrane complex may be a prerequisite for DNA synthesis. Furthermore, no M-band fraction could be found in mature unfertilized eggs—cells in which there is no DNA synthesis. When unfertilized eggs were mixed with embryos which had received a 30 s pulse during S-phase, an M-band fraction was obtained, showing that the absence of M-bands in unfertilized eggs was real. Thus the M-band seems to be formed soon after fertilization when DNA synthesis is initiated and disappears in G2 when synthesis is complete.

The M-bands and top fractions were isolated from early blastula nuclei and tested for their capacity to support DNA synthesis *in vitro*. No activity could be detected in the top fractions but the M-band fraction supported the synthesis of DNA which was dependent on the presence of all four deoxyribonucleotides.

These experiments must be interpreted with care. As suggested recently by Huberman *et al.* (*Nature*, **241**, 32 : 1973) and Fakan *et al.* (*Proc. US Nat. Acad. Sci.*, **69**, 2300 ; 1972) during cell fractionation experiments it is possible that newly replicated DNA may possess special features such as single strandedness which may cause it to bind more protein or membrane material than bulk DNA. In other words, the M-band may be an artefact of cell lysis.

the level of tertiary or of quaternary structure, that is to say by intra- or inter-chain cross-links.

LEAF MICROFLORA
Disease Control

from a Correspondent

FACTORS which influence the ecology of microorganisms on leaf surfaces were considered at a meeting of the Pesticides Group of the Society of Chemical Industry held on January 15 under the chairmanship of Dr E. Evans (Chesterford Park Research Station). The interrelationship of these factors in relation to practical disease control was indicated by several of the speakers.

The nature of the leaf surface and its microclimate may determine the success or failure of organisms to colonize foliage and these factors were surveyed by Dr B. E. Juniper (University of Oxford) and Dr S. W. Burrage (Wye College, University of London), respectively. Dr Juniper's electron micrographs of the leaf surfaces showed the marked variation in thickness and nature of cuticles and epicuticular waxes, not only between species but also between abaxial and adaxial surfaces of individual leaves. The wettability of leaf surfaces is influenced by the fine structure and chemical composition of the wax. Dr Burrage stated that the temperature and humidity at the leaf surface are determined by the balance between heat transfer by radiation, conduction and evaporation/condensation of water. The shape, size, orientation and surface topography of the individual leaf influence the boundary layer thickness and hence the energy exchange and microclimate.

The effect of the latter on spore germination and the growth of leaf microorganisms was also stressed by Dr J. P. Blakeman (University of Aberdeen). Water on foliage can release substances from leaves, especially older ones that have lost wax by weathering, and from microorganisms. He mentioned that pollen deposits on leaves stimulate spore germination and growth of *Botrytis cinerea* and of the saprophytic bacterium *Sporobolomyces pararoseus*. The latter reduced development of *Phoma betae* lesions on sugar beet foliage, probably by competing for nutrients.

Dr P. J. W. Saunders (University of Manchester) discussed the effects which pollutants may have on leaf surface microflora; for example, *Dilocarpon rosae*, which is sensitive to sulphur dioxide, will be favoured by a reduction of this pollutant as indicated by the increasing incidence of rose black spot in some areas where clean air

zones have been enforced. Dr C. H. Dickinson (University of Newcastle upon Tyne) stated that bacterial populations on foliage usually increase as leaves age. He summarized the effects of various fungicides on microflora on the surfaces of potato and barley leaves. Disturbance of the ecological system by the interactions of fungicide with different microorganisms might produce beneficial or adverse effects on the plant. One fungicide, which decreases populations of saprophytic organisms on the leaf surface, was associated with delayed foliar senescence and increased barley yields even in the absence of recognized pathogens. Dr R. T. Burchill reviewed work at East Malling Research Station showing that apple scab, caused by *Venturia inaequalis*, can be controlled by spraying orchards with a 5 per cent solution of urea after harvest but before leaf fall. He stated that the mode of action of urea is complex: it may act partly by increasing leaf populations of fungi such as *Alternaria* spp., *Cladosporium* spp. and *Fusarium* spp., all of which antagonize the development of *V. inaequalis* perithecia; moreover, urea stimulates some soil flora and increases the rate of decomposition of fallen leaves, thus decreasing the carryover to the next season of infection by perithecia.

Dr G. Barnes (Chesterford Park Research Station) has investigated the interaction of *Erysiphe polygoni* and *B. cinerea* on detached leaves of clover, *Trifolium pratense*. Dry conidia of *B. cinerea*, when placed on the leaf surface 24 hours before inoculating with *E. polygoni* conidia, slightly de-

creased germination and formation of the appressorium in the latter and reduced the production of secondary hyphae by as much as 80 per cent. No such effects occurred when conidia of *E. polygoni* were inoculated either before or simultaneously with *B. cinerea* conidia. Interactions between bacterial populations on leaf surfaces were surveyed by Dr J. E. Crosse (East Malling Research Station). He has found that inoculation of apple shoots with *Erwinia amylovora*, the bacterium causing fireblight, immediately after inoculation with a yellow bacterium, which is commonly associated with fireblight lesions, decreased infection by *E. amylovora*. Similarly, the rate of infection and spread of cherry canker, caused by *Pseudomonas morsprunorum*, is diminished by a white bacterium isolated from cherry leaf surfaces. Attempts to use saprophytic bacteria as a satisfactory biological control against these diseases have, so far, failed because their populations rapidly fall to levels non-competitive with the pathogens.

SUPERFLUIDS
Building Up the Case

from a Correspondent

IT now seems much more probable that there is a third superfluid in nature, in addition to liquid ^{4}He and the electron gas in superconductors. This is the implication of a recent report by Webb, Greytak, Johnson and Wheatley (*Phys. Rev. Lett.*, **30**, 210 ; 1973), the latest in a series of papers from both

DNA Polymerase Mutant of the Smut Fungus

SINCE the isolation by DeLucia and Cairns of mutant strains of *Escherichia coli* lacking DNA polymerase I activity two other DNA polymerases of *E. coli* have been identified and characterization of the biochemistry of DNA replication continues apace. Of course, it should be possible to make essentially similar analyses of the DNA replication machinery of at least some eukaryotes, and with this aim in mind Jeggo *et al.* screened several hundred temperature sensitive mutants of the smut fungus *Ustilago maydis*. As they report in *Nature New Biology* next Wednesday (March 7), they found five temperature sensitive mutants of *U. maydis* that were blocked in DNA synthesis at the non-permissive temperature.

DNA polymerase activity in extracts of one of these mutants was only 10–25 per cent that of wild type. Tetrad analyses indicated that the temperature sensitive phenotype of this mutant is

the result of a single recessive mutation which may well be in a structural gene for a DNA polymerase because partially purified enzyme from the mutant proved to be more thermolabile than wild type enzyme. Susceptibility to radiation damage and to chemical mutagens of the mutant strain of *U. maydis* growing at different temperatures suggests that the mutation does not affect a principal DNA repair pathway. Because, however, the mutant cells, grown at the non-permissive temperature, develop into filamentous uninucleate forms whereas wild type cells grow by budding like a yeast, it may well be that Jeggo *et al.* have been lucky and have isolated a temperature sensitive mutation which affects DNA polymerase involved in chromosome replication.

Confirmation of this possibility will depend on the results of experiments which may lead to a characterization of the replication machinery in this fungus.

sides of the Atlantic which suggest with increasing certainty that a phase transition occurs in liquid ³He near 0.002 K. This transition is closely analogous to the superconducting transition in a metal.

According to quantum statistical mechanics, the properties of a fluid at very low temperatures are determined chiefly by whether the atoms of which it is composed contain an even number of fundamental particles, in which case they are bosons, or an odd number, in which case they are fermions. The ⁴He atom (2 protons, 2 neutrons, 2 electrons) is thus an example of a boson and the ³He atom, with one less neutron in the nucleus, is a fermion. The two liquids are therefore expected to display completely different properties at very low temperatures, a prediction which was verified experimentally several years ago when ³He first became available in quantities sufficient for experiments. Superfluidity in liquid ⁴He is associated with a curious phenomenon, known as Bose–Einstein condensation, in which a substantial proportion of the atoms congregate in the same zero-energy quantum state. By contrast, the occupation of a single quantum state by more than one fermion is rigorously forbidden, so that a Bose–Einstein condensation, leading to superfluidity, cannot occur in liquid ³He.

There is, however, a completely different mechanism by which the electrons (also fermions) in a superconductor are able to acquire their superfluid properties. This is the formation of so-called Cooper pairs: where there is an attractive force between the electrons, on account of their interaction with the lattice of positive ions, the assembly can reduce its total energy by forming pairs of electrons. The scattering of electrons by lattice defects or thermal vibrations, which gives rise to electrical resistance in a normal metal, would entail breaking pairs and thus cannot occur unless a certain minimum amount of energy is available. The electrons can therefore flow through the lattice without dissipation of energy, provided that a critical drift velocity is not exceeded. In the case of liquid ³He, the possibility of attractive interactions, which might enable a similar transition to the paired state to occur, was considered more than a decade ago by several workers who estimated transition temperatures around 0.1 K. Subsequent experiments failed to reveal a transition; but more refined theories quickly pushed the predicted transition to still lower temperatures. This cyclical process has been repeated several times since then, but on each occasion the transition has failed to appear at the temperature expected.

The whole topic attracted renewed interest last year when Osheroff, Gully, Richardson and Lee (*Phys. Rev. Lett.*, **29**, 920; 1972) reported evidence of some sort of phase transition in liquid ³He under high pressure near 0.002 K. Unfortunately, however, their data were hard to interpret in detail because their cooling technique meant that, inevitably, some solid ³He was also present in the experimental cell.

The experiments by Webb *et al.* made use of a different cooling method, and provide the first clear indication that the phenomenon observed by Osheroff *et al.* is indeed the long-awaited transition to a paired state: they find that no latent heat is associated with the transition, but that there is a finite discontinuity in the specific heat. This behaviour is characteristic of a second-order phase transition, the only other known example of which is the superconducting transition in a metal.

Does the new phase of liquid ³He have superfluid properties? Observation of the second-order phase transition leaves little doubt that there are close similarities between this new phase and the electrons in a superconductor, but clearly there are also profound differences. In a superconductor the fermions are negatively

Integrating Two Unrelated DNA Sequences

MOST bacteriophage DNAs which can be inserted into the chromosome of a bacterial host on infection can integrate at only one, or at least a very few, sites in the bacterial genome. A striking exception is provided by phage mu, which can integrate at any point in the chromosome of *Escherichia coli*. When it inserts within a gene, the bacterium behaves as mutant lacking the gene function. This unusual activity has already been put to practical use by Nomura and Edbaek (*Proc. US Nat. Acad. Sci.*, **69**, 1526; 1972) to map the relationship of the genes coding for ribosomal proteins and by Louarn, Bird and Caro (*J. Mol. Biol.*, **70**, 549; 1972) to demonstrate the bidirectional replication of the *E. coli* chromosome.

The mechanism of this integration is analysed in an article by Toussaint and Faelen in *Nature New Biology* next Wednesday (March 7). They have taken advantage of their previous observation that phage mu can promote the integration in the bacterial chromosome of a defective lambda phage (which usually inserts at one specific site) unable to integrate of its own accord. If the lambda phage carries an active *gal*⁺ gene, its integration is marked by the restoration to infected cells (of the *gal*⁻ genotype) of ability to metabolize galactose as a carbon source.

The question which Toussaint and Faelen answer is whether mu promotes the integration of lambda simply by providing some enzymatic activity or whether the two DNAs are physically linked in some way so that lambda is inserted at the same site as mu. They have therefore isolated cells in which λ*gal*⁺ has been inserted within a bacterial gene (by screening for the inability of the cell to provide the metabolic activity coded by that gene). The next step in the analysis is to see which of the integrated phages is lost if the bacterial gene bearing these insertions is replaced by a normal, functional bacterial gene. This experiment is performed by transducing the cells with a P1 phage.

In a *his*⁻ *E. coli* strain which had received λ*gal*⁺ and mu, transduction to provide a normal *his*⁺ bacterial gene resulted in the loss of both λ*gal* and mu. This implies that both phage DNAs must have integrated at the same site, within the *his* gene. In further experiments, the chromosomes of cells bearing λ*gal*⁺ were transferred by conjugation into *gal*⁻ bacteria. All the *gal*⁺ recipients received both the lambda and mu DNAs, which supports the idea that mu enables lambda to integrate because the two phages are linked together in some way. In these different strains, the *gal*⁺ was located at widely differing points in the donor chromosome, showing that mu retained its usual capacity to integrate at any point, the integration of λ*gal* taking place at the same site.

The model which Toussaint and Faelen propose to explain these results is to suppose that two phage mu DNAs are implicated in the integration process. The two mu DNAs interact with each other at the specific sites which the phage uses for integration to form a dimer. One of the two sites of this dimer integrates in *gal* DNA; the other integrates in the bacterial chromosome. The result is that the bacterial insertion site carries a λ*gal* genome, surrounded on each side by a mu genome. Studies of the structure of the DNA which is inserted support this model. The use of mutants in phage mu shows that the same phage functions are implicated in its interaction with λ*gal* and with bacterial DNA.

One implication of this model is that in principle it should be possible to utilize mu to connect together any two circular pieces of duplex DNA in the bacterial cell. Although this model is consistent with the genetic data, biochemical confirmation of the proposed DNA interactions will be needed before it can be put to such interesting and important uses.

charged electrons moving through a lattice of positive ions whereas, in the case of ^{3}He, there is no lattice and the fermions are neutral atoms. It is not obvious, therefore, just how far the analogy can be taken.

SOLID STATE

Laser Writing

from a Correspondent

THE past four or five years have seen a great increase in research on amorphous semiconductors. This has followed a rather longer period devoted to crystalline materials and the development of very sophisticated semiconductor devices. Amorphous materials have been investigated principally in the form of glasses, and the particular property that has, perhaps, stimulated the most interest is their electrical behaviour. Devices made from such materials show either memory or threshold switching depending on their composition. (Memory switching is the phenomenon by which the material may exhibit either a high.or a low resistance state.)

It is now fairly certain that memory switching is associated with the transition from amorphicity to a crystalline state, in the form of thin filaments between the electrodes caused by electrical heating followed by slow cooling. The reverse process involves heating followed by a rapid cooling or quenching to allow the material to devitrify or revert to the amorphous state.

It is now possible to induce a similar condition in amorphous materials by the interaction with light from lasers. Rapid crystallization and equally rapid devitrification of amorphous chalcogenides (for example $Te_{81}Ge_{15}Sb_2S_2$) have been observed when they are exposed to short laser pulses (*Appl. Phys. Lett.*, **18**, 254 ; 1971). This process of optical switching is made evident by the sharp change in the optical transmission and reflexion properties of those areas so exposed. It was suggested that the physical change is attributable to a bond-weakening mechanism or photocrystallization process, but a more recent paper (*Appl. Phys. Lett.*, **22**, 48 ; 1973) gives evidence that in a similar glass the initial devitrification is temperature activated. This paper also shows how by using the same laser it is possible to produce a crystalline area (memory state), to measure the change in optical transmission (read out), and to revert the same area to the amorphous state (erase).

These optical memories can also be operated in the so-called "reverse mode" (*J. Appl. Phys.*, **43**, 4688 ; 1972). An initial uniform crystalline state is obtained by heating the glass thin film to 90° C. The interaction with laser light produces an amorphous pattern which can be first "read" and then "erased" by heating once more to 90° C and cooling slowly. The advantages of this reverse mode of operation are that it gives a much faster "write time", allowing the rather slower reverse process to be used for "erasing".

It is very difficult at this stage of their development to predict the future for these devices, but undoubtedly they will be the subject of many more investigations, if only to resolve further the mechanisms involved in this phenomenon.

SAN ANDREAS FAULT

Pore Pressure and Creep

CREEP occurring in the central part of the San Andreas Fault—a right-lateral strike-slip fault running through California—can be related to changes in the pore pressure of water, as measured in a well 150 m deep, near Hollister. In this part of the fault the total creep of 1.2 cm yr^{-1} occurs as a series of small creep events.

Johnson, Kovach, Nur and Booker report (*J. Geophys. Res.*, **78**, 851 ; 1973) that both the maximum pore pressure and the offset in water level in the well are linearly related to the total creep in motions which occur within hours of anomalous changes in water level.

Three creep events, of magnitudes 4 mm, 3 mm and 2 mm, were associated with changes in water level of $+5.6$ cm, -4.1 cm and $+3$ cm, respectively. The water level started to change 4 h before the first event, 1.5 h after the second and 8 h before the third. The recorder used is sensitive only to within ± 2 mm, insufficient for changes caused by Earth tides, for example, to have been monitored. The one to one correspondence — all anomalous water level changes were associated with fault movement—is particularly striking, and follows several recent experiments, notably in Colorado, where earthquakes have been produced by deliberate injection of water into the pores.

The success of those experiments has led to speculation that it might be possible to make the San Andreas Fault safe by drilling deep wells along the fault line and "locking" it by pumping water out. Selected regions of the fault could then be isolated and water pumped in to liberate the slip. Repeated small man-made earthquakes could ensure a relatively smooth slip without the sudden massive jerks which make the region so dangerous at present—or so the argument runs.

Johnson *et al.* point out that it is not possible, as yet, to say whether the transient pore pressure is produced by creep or the creep by changes in fluid levels. But deeper wells might be able to detect strains and pressure changes deeper in the Earth, monitoring pore pressure changes at different distances from the active region of the fault. If such monitoring proves effective, it may become possible to predict some of the behaviour of the active fault, or to understand the delicate balance of pore pressure and fault activity sufficiently well to permit experiments aimed at stabilizing the fault, by adding or removing water as required. That, however, is certainly a very long term prospect indeed.

Doppler Measurements of Metal Flow Velocities

ULTRASONIC Doppler velocimeters have been found useful in the measurement of fluid flow, for example blood flow. The technique depends, of course, on the presence of inhomogeneities in the fluid, from which the sound waves can be reflected. This would seem to make the technique unsuitable for studying liquid metal flow, but in the best traditions of "suck it and see" Fowlis has attempted to use such a velocimeter to measure the flow of both mercury and the liquid alloy NaK (47 per cent Na by weight, 53 per cent K). To his own surprise, he obtained a strong Doppler signal for both metals (see next Monday's *Nature Physical Science*, March 5).

The photograph shows the apparatus used, in which the Doppler shift of ultrasonic waves backscattered from the moving metal is recorded. The metal flows under gravity between two reservoirs along a tube in which the ultrasonic probe is mounted. The Doppler shift frequency range can be directly examined with the analyser and oscilloscope to the left.
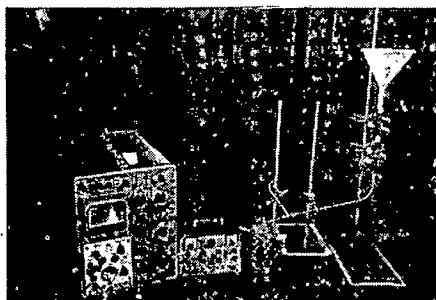
The source of the backscatter is unknown, although Fowlis does point to dust particles or microscopic bubbles as possible candidates ; the important practical point, however, is that the system offers a cheap and apparently accurate means of measuring such flow, no matter how the effect works.

SELENOLOGY

Lunar Seismology

from a Correspondent

A CONFERENCE on geophysical and geochemical exploration of the Moon and planets was held at the Lunar Science Institute, Houston, Texas, on January 10 to 12. Although most of the contributions concerned the Earth-based research that had been pursued in recent years, some of the results presented were obtained from the Apollo programme, and there were even some very preliminary data from Apollo 17.

The first contributions, presented by Drs G. Latham and M. N. Toksöz (University of Texas, Galveston) and others, were concerned with the very interesting picture of seismicity that is emerging from the four Apollo seismograph stations now operating on the Moon. It seems that although the Moon is very seismically inactive by comparison with the Earth there is sufficient natural activity (arising from surface impacts and internal sources) for it to be possible to draw a firm outline of the Moon's internal seismic properties within the expected lifetime of this network. Judged as yet only by a very remarkable repetition of the waveforms of discrete events in the seismograms, some forty internal sources that must be very precisely located have now been identified. Only a few of these sources have been given a position within the Moon, but they all seem to be in a zone 600 to 1,000 km deep and there is some evidence that they tend to be immediately below the boundaries of the maria that are associated with mascons. In spite of the primitive state of the data there was talk of this seismicity being the result of mascons dropping back into the Moon—the whole process being triggered by the tidal effects of the Earth. In this connexion it is interesting that the results of laser altimetry from orbiting spacecraft presented by Dr W. R. Wollenhaupt (NASA, Houston) have shown that the sites of mascons are among the lowest places on the Moon's surface. From the study of a few impacts on the far side Dr Y. Nakamura (University of Texas, Galveston) reported that there seems to be a region of relatively high attenuation, with Q no greater than that of the Earth's upper mantle, below a depth of (approximately) 1,000 km.

Problems relating to the character and origin of lunar magnetism continued to attract attention. Information returned from the Apollo 15 and short-lived Apollo 16 sub-satellites travelling in near equatorial orbits, and presented by Dr P. J. Coleman (University of California, Los Angeles), shows that there is a highly structured lunar magnetic field (length scale tens

to hundreds of kilometres) detectable at heights generally less than 100 km. This ties up with the few spot readings taken on the surface. As with the surface topography there seems to be a systematic difference in the character of this field on the near and far side, and there was continuing debate about the way such a field will influence the interaction of the solar wind throughout a synodic month. The cause of this field can be reasonably attributed to the observed remanence of the surface rocks, but the origin of that remains undecided. It only need be added that the discovery of high attenuation in an extensive central region of the Moon, combined with the celebrated lunar reverberation, makes the problem of demonstrating seismically the existence of a small dense core suitable as a site for a lunar dynamo that much more difficult. More results were presented by Dr T. Nagata (University of Tokyo) and Dr G. R. Olhoeft and his colleagues (NASA, Houston) on the electrical conductivity of lunar material under conditions relevant to the interpretation of very shallow and deep electromagnetic sounding of the Moon. Although in the earliest measurements on lunar rocks it seems that enough attention was paid to oxidation of the samples at high temperatures, the latest data do not affect the earlier result that the temperatures deep within the Moon may be no more than 1,000° C.

Interesting contributions were given by Dr C. R. Chapman (Planetary Science Institute, Tucson) and Dr T. B. McCord (MIT) on the analysis of the surface material of various bodies in the Solar System by spectrometric analysis of reflected light. There seems to be enough structure in some of the spectra to indicate differing compositions among the asteroids—some with no meteoritic equivalent. The absence of structure in the spectra of some of the largest asteroids is similar to that of basalt, and suggests that some of these may be chemically differentiated. There were also contributions on the interpretation of photographs of the Martian surface taken on the recent Mariner 9 flight.

Nigerian Thermal Plume Traces

IN next Monday's *Nature Physical Science* (March 5), van Breemen and Bowden report systematic geochronological data in respect of four Nigerian subvolcanic granites. These support the idea that igneous chains are thermal plume traces on moving lithospheric plates.

The non-orogenic granitic ring complexes of the Nigeria–Niger province, which form a narrow intrusive zone about 1,300 km long down longitude 9° E, fall into three geographical groups near Air, Zinder and Jos, respectively (see map). The central Nigerian complexes around Jos have previously been taken to be close to 160 million years old. The new, more detailed rubidium-strontium studies of van Breemen and Bowden, however, give a geographical pattern of ages ranging from 117 m.y. for the Liruei complex (*c* on the map), through 167.5 m.y. for the Amo complex (*f*) to 156 m.y. for the Pankshin complex (*h*). If this age range is taken to be the result of a plume trace, there is a clear implication here that at the relevant time Africa drifted northwards at a rate of about 0.76 cm a year—a conclusion which contradicts the suggestion from Burke and Wilson (*Nature*, **239**, 387; 1972) that Africa underwent a Mesozoic standstill.

Van Breemen and Bowden then discuss the consequences of the assumption that the other Nigeria–Niger granite complexes reflect plume traces. For example, the rate of 0.76 cm per year extrapolated to northern Air gives an age of about 300 m.y., which agrees with unpublished potassium–argon age

determinations, although extrapolation to other granites at Hoggar, further north, leads to a discrepancy of about 200 m.y. between predicted and observed ages. Another feature of the Jos area granites which requires explanation is the two different trends represented by *a-d* and *i-k*, on the one hand, and *c-h* on the other. Van Breemen and Bowden tentatively suggest that these changes in trend reflect changes in the direction of Africa's motion relative to the breakup of Pangea.
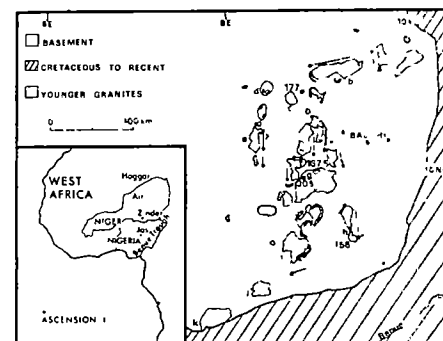
Some geologists have related the Nigerian granites to a plume now thought to lie beneath Ascension Island, although there is apparently no seamount chain linking the island to Nigeria. Van Breemen and Bowden end by showing that palaeomagnetic data, plate tectonics and the motion of Africa predicted from the postulated Nigeria–Ascension Island plume trace are consistent, suggesting that little polar wandering has occurred since the mid-Jurassic.

QUASISTELLAR OBJECTS

Are All QSOs in the Nuclei of Galaxies?

by our Cosmology Correspondent

"ALL quasars occur in the nuclei of giant galaxies"—or, at least, "the observations are consistent with the hypothesis", according to Jerome Kristian, of the Hale Observatories. Coming close on the heels of the recent report that the QSO redshift-magnitude relation agrees well with the idea that these objects are at the cosmological distances implied by a Doppler interpretation of the redshifts (see *Nature*, **241**, 506; 1973), this discovery seems to have brought QSOs back into the limelight of astronomy, after a period in which the centre of the stage has been held by objects closer to home, within our own Galaxy.

Kristian's study (*Astrophys. J. Lett.*, **179**, L61; 1973) starts from the often discussed similarity between N galaxies, Seyfert galaxies and QSOs. These objects not only have the same qualitative properties, in terms of spectra, colours and variability, but also show a quantitative gradation in activity. This has led to speculation, for example, that the objects might be members of an evolutionary chain in which QSOs are the forerunners of Seyfert galaxies which in turn evolve into N galaxies. That idea does not stand up too well if there is no evidence for luminosity evolution of QSOs as a class, which now seems to be the case (Bahcall and Hills, *Astrophys. J.*, **179**, 699; 1973). Instead, the idea that QSOs are events occurring in the nuclei of galaxies, like those observed in the nuclei of N and Seyfert galaxies, becomes attractive. In that case, QSOs could easily be so much brighter than the equivalent events in N and Seyfert galaxies that their light output masks the light from the galaxies in which they lie, so that the characteristic starlike image of a QSO is produced on photographic plates. This is the idea that Kristian set out to test, using direct photographs of QSOs in an attempt to detect galaxies surrounding them. The results he obtains are impressive.

In order for such a photographic search to be successful, the image produced by a QSO at the centre of a galaxy must be smaller than the image produced by the galaxy itself. The QSO image size depends only on brightness, because QSOs are essentially point sources, but the galaxy image size depends on the actual size of the galaxy and its distance from the observer. This provides enough flexibility to make a photographic search for QSOs at galactic nuclei—or rather, galaxies centred on QSOs—feasible.

Kristian has taken the QSO redshifts as straightforward distance indicators, and has used calibrations of image size against magnitude for the QSOs and of apparent size against redshift for the galaxies. The latter calibration was already available from Sandage's work on brightest members of galaxy clusters (*Astrophys. J.*, **173**, 485; 1972); the former calibration was made by Kristian using V plates obtained with the 200-inch telescope. QSOs are usually identified from the *Palomar Sky Survey*, which is based on plates obtained with the 48-inch Schmidt camera. Underlying galaxies are not usually found associated with QSOs on the Schmidt plates, and it now seems that this is simply because, at the distances implied by QSO redshifts, galaxies are, in most cases, too small to produce an image larger than the QSO image on 48-inch plates.

Kristian has restricted his survey to objects which "have at one time or another been called quasars, and for which 200-inch plates or other indications of an underlying galaxy are available"; this gives twenty-six objects for analysis. In regions of the Hubble diagram where galaxies should be easiest to detect there are few QSOs (four were studied by Kristian) "but all of those for which good plate material is available show an underlying galaxy". These galaxies all satisfy the requirements of N galaxies, although because of the historical accident of discovery some are known by other names.

At the other extreme, where galaxies which are centred on QSOs should be difficult to detect none is found, although there are fourteen QSOs which satisfy Kristian's criteria, and in intermediate regions of the Hubble diagram there is evidence that five out of eight QSOs are at the nuclei of galaxies. The apparent diameters of the galaxies are as would be expected for N galaxies and bright cluster galaxies, and there are, says Kristian, also several cases in which the QSO is a little displaced from the centre of the galaxy rather than coincident with the nucleus. The evidence is impressive, but, of course, some QSOs may still not be at galactic centres.

Spin, Torsion and Gravitational Singularities

THE big-bang model of the Universe contains a singularity which is interpreted as the beginning. This is unsatisfactory in one way because the details of physical processes near to singularities are not well understood. It is, however, clear that quantum effects become important at high densities, although how to incorporate these effects into gravitational theory is an open question.

Oscillating models of the Universe also collapse periodically into singularities. The most obvious explanation is their very high symmetry and it would seem that the periodic collapse would be avoided if the model were slightly perturbed, allowing the incoming particles of matter to miss each other. Calculations by Penrose, Geroch and Hawking have, however, shown that this is not the case and that singularity is an intrinsic feature of general relativity which occurs under quite wide conditions subject only to very general and reasonable energy conditions.

General relativity therefore needs to be modified if singularities are to be avoided. Such a modification was suggested by Cartan and by Sciama in 1958 and incorporates an asymmetrical connexion to provide a model of spin. The cosmological consequences of this idea are worked out in next Monday's *Nature Physical Science* (March 5) by Trautman. In his communication the field equations of general relativity are modified by the presence of terms describing the torsion of the geometry arising from the spin of particles. Recently Kopczynski constructed nonsingular models, based on the resulting modification of the Friedmann equations describing the expansion of the Universe according to the big-bang model. It turns out that there is a minimum radius for the 10^{80} particles of which the Universe is thought to consist. This radius is about 1 cm— quite large enough to avoid the difficulty of singularity, but small enough to have a negligible effect on the subsequent development.

Trautman considers the possibility that the spins were correlated in the hottest stage of the development of the Universe; the cosmic magnetic field might have played a significant part in this context. Trautman's is not a complete model, however, in that it neglects the magnetic field energy. Pressure is also ignored in the preliminary calculation.

Trautman also mentions the possibility of avoiding a singularity in a closed cosmological model. It is interesting to note the similarity of his modified Friedmann equations to those proposed some years ago in a continuous creation model of an oscillating universe by Hoyle and Narlikar.

T and B Lymphocytes and Immune Responses

MARTIN C. RAFF

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> The recognition of two distinct classes of lymphocytes has been a turning point in immunology. Immunological models and tools may help to provide the answers to many biological problems.

IMMUNOLOGY has become an exciting science of its own. Nonetheless, what is being learned about lymphocytes and the immune responses that they mediate has important implications for medicine and other branches of biology. Unfortunately, the private language of immunology has made it difficult for non-immunologists to join in the excitement. This article attempts to review what is known in general terms about the cellular basis of immunity. (For a more detailed review of lymphocytes and their roles in immune responses, see ref. 1.)

Immunology is concerned with the specific responses an animal makes when foreign materials (antigens or immunogens) are introduced into its body. Such immune responses are made by all vertebrates and consist of the production of specific immunoglobulin protein molecules (antibodies) and/or specifically reactive cells, both of which can circulate in the blood and react specifically with antigen. As a result of this reaction, the foreign material may be inactivated (for example, bacterial toxins), killed (for example, infecting organisms or transplanted cells) and/or phagocytosed by cells of the reticulo-endothelial system. On the other hand, in some cases, such immune responses may have deleterious effects on the host, such as in hypersensitivity reactions (hayfever and drug allergy, for example), where antigen reacting with antibody fixed to basophils and mast cells causes the release of histamine and other pharmacological mediators of inflammation. In general, immune responses which can be transferred to another animal by means of serum from a sensitized donor (containing antibody) are termed humoral immune (or antibody) responses, whereas those that can be transferred by sensitized cells but not by serum are called cell-mediated immune responses.

While immunochemists were unravelling the structure of antibody in the 1950s and early 1960s, cellular immunologists were demonstating that lymphocytes are the principal cells involved in immune reactions. The most convincing experiments were those showing that relatively pure populations of rat lymphocytes obtained from the chief lymphatic vessel, the thoracic duct, could transfer both cellular and humoral immunity to irradiated rats, which could not respond immunologically themselves as their lymphocytes had been killed by the radiation (reviewed in ref. 2). In addition, depleting animals of lymphocytes by prolonged drainage of the thoracic duct was found to impair their immune responsiveness[2]. Thus lymphocytes, whose origins and functions had been a mystery for so long, were established as "immunocompetent" cells.

It was soon realized that lymphocytes are not a homogeneous population. Several lines of evidence suggested that there are two distinct types of immunocompetent lymphocytes: one which requires the thymus gland for development and is responsible for cell-mediated immunity and another which develops independently of the thymus and mediates humoral antibody responses. The evidence came from studies in birds, rodents and man in the 1960s. In birds[3,4] and rodents[5] it was found that removing the thymus from an embryo or newborn markedly impaired the cell-mediated immune responses of the animals when they grew up, but had much less effect on humoral immunity. On the other hand, removal at hatching of the bursa of Fabricius[3,4], a cloacal lymphoid organ unique to birds, impaired the bird's ability to make antibody, but had little effect on cell-mediated immunity. Investigations of patients with immunological deficiency diseases also showed that humoral and cell-mediated immunity could be separately affected (reviewed in ref. 6): patients with Bruton-type congenital agammaglobulinaemia could not make antibody and were deficient in lymphoid cells producing antibody, but had normal cell-mediated immunity, whereas children with congenitally hypoplastic thymus glands (for example, Di George's syndrome) had markedly impaired cell-mediated immunity but could make relatively normal amounts of antibody in response to some antigens.

In the past few years the two-lymphocyte model of immunity has been firmly established (at least in birds and mammals), with two "central" lymphoid organs—the bursa, or its mammalian equivalent (still unidentified), and the thymus—producing lymphocytes independently of antigen, and seeding them out to the "peripheral" lymphoid organs (that is, lymph nodes, spleen and gut-associated lymphoid tissues) where they await contact with antigen which will induce them to differentiate into "effector" cells (see later). In the peripheral lymphoid tissues the lymphocytes derived from thymus are referred to as T cells, while those derived from the bursa in birds, or its equivalent in mammals, are called B cells[7].

Phylogeny

Until recently it was thought that specific immune responses were confined to vertebrates. There is now evidence, however, that some invertebrates, such as annelids and tunicates, can reject foreign tissues and that these primitive immunological responses can display specificity and possibly short-term memory[8] (that is, an increased and/or faster response on second exposure to the same antigens). These reactions are mediated by macrophage-like cells (coelomocytes) and possibly by soluble effector molecules having relatively little specificity[8]. As there is no evidence that invertebrates have lymphocytes or immunoglobulins, it seems likely that specific cellular immunity evolved before the appearance of these two principal mediators of vertebrate immunity.

All vertebrates have lymphocytes and probably thymus tissue (at least at some stage in their development) and are capable of producing antibody and cell-mediated immune responses[8]. Lower vertebrates (lampreys and hagfish, for example) have little organized lymphoid tissue and can produce only one class (IgM-like) of antibody. Rudimentary lymph node-like structures are first found in Amphibia which make two classes of antibody. Birds are the first vertebrates in which a clear dichotomy of the lymphoid system has been established, and are unique in having two discrete central lymphoid organs, thymus and bursa, producing T and B lymphocytes respectively. Mammals have abundant and highly organized lymphoid tissues, can elaborate a variety of different classes of antibody (such as IgG, IgM, IgA, IgE, IgD in man) and have distinct T and B lymphocyte populations, although the site of B cell development is still uncertain. It is not known whether vertebrates below birds have separate classes of T and B cells.

Development of T Lymphocytes

In most animals, lymphocytes first appear in the foetal thymus. The thymus anlage is composed of epithelial cells and is derived from the third and fourth pharyngeal pouches. Although in the past it had been suggested that thymus lymphocytes (thymocytes) develop from thymus epithelial cells, experiments in chickens and mice have clearly established that haemopoietic stem cells from foetal yolk sac and liver migrate into the thymus anlage and there proliferate and differentiate into thymus lymphocytes, presumably under the inductive influence of the thymus epithelium[9]. In mice (gestation 20 days) the first stem cells, which seem to be large basophilic blast-like cells, arrive in the thymus around day 11, and the first small lymphocytes are seen by day 15 or 16 of embryonic life[9]. Using radioactive[10], chromosome[5,11] and surface antigenic[9] markers, it has been shown that lymphocytes migrate from thymus to peripheral lymphoid tissues to make up the T lymphocyte population. Although this begins just before birth in mice, most of the seeding occurs in the first week of life[9]. Therefore, if the thymus is removed in the first days of life the mouse will grow up with a marked deficiency of T cells and thus impaired cell-mediated immunity, whereas thymectomy done later in life has much less effect[5]. In adult animals, stem cells from bone marrow migrate to thymus, and thymus lymphocytes continue to seed to the periphery, but these processes take place at a much reduced rate by comparison with the foetus and newborn[5,11].

Most thymus lymphocytes are immunologically incompetent (that is, they cannot respond to antigen) and differ in other ways from peripheral T cells, suggesting that there is another differentiation step from thymocyte to T lymphocyte. Recently it has been demonstrated that there is a small subpopulation (~2 to 5%) of thymus cells, located in the thymus medulla, which is immunologically competent and has most of the properties of peripheral T lymphocytes[9,12,13]. This suggests that the second differentiation step may occur within the thymus and that T cell development may be visualized as stem cell→thymocyte→"mature" thymus lymphocyte→peripheral T lymphocyte (Fig. 1). This scheme is almost certainly an over-simplification, however, for there is some evidence that cells may leave the thymus at varying stages of maturation, or perhaps as distinct cell lines, giving rise to subpopulations of peripheral T cells with different properties and functions[13]. In addition, the role of putative thymus humoral factors or hormones (thymosin, for example) is still unclear, although there is evidence that they probably do not induce stem cells to differentiate to lymphocytes outside the thymus, but may influence peripheral T cells in some way[14].

Development of B Lymphocytes

In birds, B cell development is dependent on the bursa of Fabricius which arises as a sac-like evagination of the dorsal wall of the cloaca on day 5. Chromosome marker studies have shown that stem cells (morphologically identical to those seen in the foetal thymus) begin to migrate from yolk sac to the bursa around days 12 to 13 and there differentiate to lymphocytes within 1 or 2 days[9]. By day 14, bursa lymphocytes with IgM on their surface can be seen, and bursa lymphocytes bearing IgG are seen a few days later[15]. The migration of bursal lymphocytes to peripheral lymphoid tissues has been demonstrated by isotope labelling experiments. Embryonic bursectomy results in marked depletion of peripheral B lymphocytes and a marked impairment in antibody (that is, immunoglobulin) production[15]. Recently it has been found that injecting anti-μ antibody (that is, specific for the heavy chains of IgM) before hatching, combined with neonatal bursectomy, suppresses later production of IgG as well as IgM[15]. This suggests that even B cells that will eventually produce IgG initially express IgM on their surface, and is strong evidence for an IgM→IgG switch within individual B cells. Whether this switch is driven by antigen, as suggested

by experiments in mice[16], or occurs independently of antigen stimulation, as suggested by experiments in chickens[15], is unsettled.
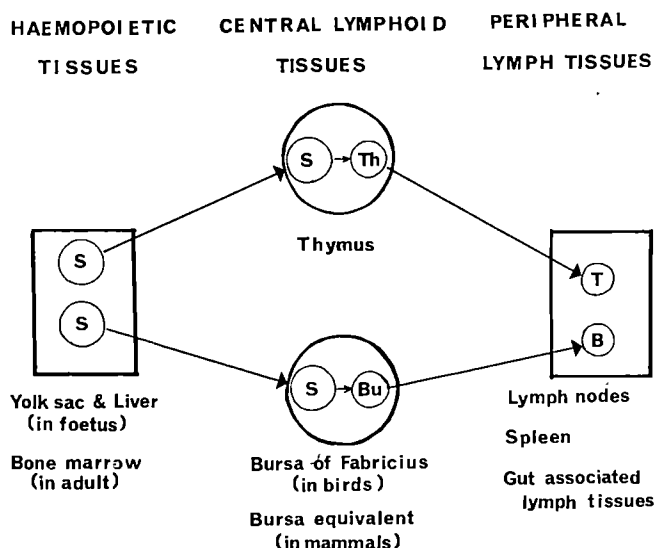
Fig. 1 Diagrammatic (and oversimplified—see text) representation of T and B lymphocyte development showing migration of stem cells (S) to thymus and bursa where they differentiate to thymus (Th) and bursal (Bu) lymphocytes, some of which migrate to the peripheral lymphoid tissues as T and B lymphocytes respectively.

In mammals, it is still not clear where stem cells differentiate to B-type lymphocytes, although it is known not to be in the thymus. It has been suggested that gut-associated lymphoid tissues (like Peyer's patches, tonsils, appendix, and so on) may serve as "bursa-equivalent", but there is little evidence to support this. In rodents, at least, there is increasing evidence that lymphocytes are produced in large numbers in the haemopoietic tissues themselves[17] (that is, liver in embryos and bone marrow in adults) and it seems likely that these tissues not only supply the stem cells for both T and B cell populations but are also the sites where stem cells differentiate to B-type lymphocytes.

It is not clear at what stage stem cells are committed to becoming lymphocytes or to becoming T or B cells. The finding of multipotential haemopoietic stem cells (that is, cells capable of becoming any of the mature blood cell types, lymphoid or myeloid) in early mouse embryonic thymus[18] suggests that commitment may not occur until stem cells enter the microenvironment of the thymus or bursa (or bursa equivalent).

Distinctive Properties of T and B Lymphocytes

As resting T and B lymphocytes are morphologically indistinguishable and are found together in all peripheral lymphoid tissue, it has been essential to find ways of distinguishing and separating them in order to study their individual properties. The demonstration of important surface differences between them has been particularly useful in this regard. Some of these surface differences can be recognized by antibody[19]. For example, the θ alloantigen (defined by alloantibody made in one strain of mouse against thymocytes of another strain) is present on mouse thymocytes and T cells, but absent from B lymphocytes, and this has proved to be a convenient surface marker for T cells in mice[19]. On the other hand, readily demonstrable surface immunoglobulin (Ig) (refs. 20, 21) and the heteroantigen, "mouse-specific B lymphocyte antigen" (MBLA) (ref. 19)—defined by hetero-antibody made in rabbits against mouse B cells—can serve as B cell markers. With antisera reacting specifically with the surface of one or other lymphocyte

type, either cell population can be killed in the presence of complement, and thus eliminated from a cell suspension. Alternatively, one can use antibody on digestible solid-phase immunoabsorbents[22], or fluoresceinated antibody and fluorescence-activated electronic cell sorting[23], to purify either type of cell. In addition to surface antigenic differences between T and B cells, the latter can bind antibody-antigen-complement complexes by means of surface complement receptors[24], and antibody-antigen complexes by means of receptors for the Fc part of complexed Ig[25]; resting T cells do not have these receptors. The functions of Fc and complement receptors on B cells are unknown, but it has been suggested that they may be important in antigen localization in the lymphoid tissues, in B cell activation by antigen and/or in putative killing by B cells of target cells coated with antibody.

Most T lymphocytes continuously recirculate between blood and lymph, passing out of the blood through specialized post-capillary venules in lymph nodes and Peyer's patches, passing through the substance of the lymphoid tissues and entering the efferent lymph; they then re-enter the bloodstream by way of the thoracic duct[2,5]. Although most B lymphocytes seem not to recirculate, some apparently do, but through different areas of the lymphoid tissues and with a slower transit time than T cells[26]. In the peripheral lymphoid tissues, T and B cells are found in more or less separate areas, the so-called thymus-dependent areas (periarteriolar sheath of spleen, para-cortex of lymph nodes, and interfollicular areas of gastro-intestinal lymphoid tissues) and thymus-independent areas (lymph follicles and peripheral regions of splenic white pulp, follicles and medulla of lymph nodes and follicles of gastro-intestinal lymphoid tissues) respectively[27]. When radiolabelled T or B cells are injected into an animal, they migrate specifically to their respective areas[27]. Although both T and B lymphocyte populations are heterogeneous[1], T cells have a longer generation time[28] on average and are slightly larger[29], more dense[24], less adherent[24] (to various materials such as glass, plastic, nylon, and so on) and more negatively charged than B cells[30]. In addition, T lymphocytes are preferentially depleted by anti-lymphocyte serum[31] (which acts principally on recirculating cells), but in general are less sensitive to cytotoxic drugs (for example, cyclophosphamide[32]), corticosteroids[33] and irradiation[34]. T and B cells also differ in their in vitro responses to a variety of "mitogens", such as plant extracts (phytomitogens), bacterial products (like endotoxin) or antibodies to lympho-cyte surface antigens, which stimulate a relatively large proportion of T and/or B lymphocytes to divide and differentiate into blast cells. Although pokeweed stimulates both T and B cell proliferation, concanavallin A (Con A), phytohaemag-glutinin (PHA) and lentil stimulate only T cells, and lipopoly-saccharides (for example, E. coli endotoxin) and anti-Ig sera stimulate only B cells[35]. It is of interest that although soluble Con A and PHA selectively activate T cells, they bind equally well to B cells, and if covalently linked to solid-phase materials they stimulate B cell proliferation[35]. Mitogen stimulation of lymphocytes is being intensively studied as a possible model of lymphocyte activation by specific antigen. These studies have made it clear that there is more to lymphocyte activation than simple binding of ligand to surface receptors.

Antigen Recognition and Specific Lymphocyte Receptors

The central dogma of immunology is the clonal selection hypothesis which suggests that at some time in ontogeny and independently of antigen, individual lymphocytes (or clones of lymphocytes) become committed to responding to one, or a relatively small number of antigens; they express this commitment through antigen-specific receptors on their surface. Thus, when an antigen is introduced into the body it selects out those lymphocytes which already have receptors for the antigen on their surface; the interaction of antigen with receptors initiates the activation of the specific cells. There is

now an impressive body of evidence supporting the clonal selection hypothesis for both T and B lymphocytes. Thus T and B cells have been shown to bind antigen to their surface[36] (although it has been more difficult to demonstrate T cells binding antigen than B cells) and in general only a small proportion of lymphocytes (~ 1 in 10^4 to 10^5 in unimmunized animals) bind any one antigen. Furthermore, if lymphocytes are exposed to a highly radioactive antigen, both T and B cell responses to that antigen can be selectively abolished, while responses to other antigens are unaffected[37]. Similarly, B cells capable of responding to a particular antigen specifically adhere to glass beads coated with the antigen and can thus be specifically removed from a cell suspension[38]. Although T cells tend not to adhere under these conditions[38] for reasons that are unclear, T cells responsive to cell surface alloantigens can be selectively removed in cell monolayers bearing the specific alloantigens[39].

In 1900, Ehrlich proposed that cells producing antitoxins (now known to be B cells) had antitoxin molecules as receptors on their surface. The more recent version of the receptor hypothesis suggests that B lymphocytes have antibody molecules (that is, Ig) as receptors for antigen, which, at least in their combining sites, are identical to the antibody which the cell or its progeny will eventually secrete. There is now good evidence for this view, in that B cells have been shown to have Ig molecules on their surface ($\sim 10^4$ to 10^5 a cell) (refs. 20, 40) and anti-Ig antibody inhibits their ability to bind or respond to antigens (reviewed in ref. 1). There is also increasing evidence that the antigen-specificity of receptors and secreted antibody are the same for any one B lymphocyte clone[41,42]. The Ig class of the receptors and that of the ultimately secreted anti-body may not, however, always be the same, for B cell pre-cursors of some IgG secretory cells seem to have IgM receptors[15,16]. As different antibody classes (for example, IgG and IgM) seem to be able to share the same specificity (that is different Ig constant regions can be associated with identical Ig variable regions[43]) an IgM→IgG switch within a single clone need not imply a switch in specificity. In mice, at least, there is some evidence that most virgin B cells have IgM receptors (in its 7–8S monomeric form[44]) which may switch class after a primary exposure to antigen[16]. The more funda-mental question of how antibody diversity is generated, that is how an animal develops the ability to synthesize such a large number of different Ig molecules (receptors and secreted antibodies) is still being debated. Germ-line theories. which suggest that one is born with a large number of variable region Ig genes, are competing with various somatic theories, which postulate that one is born with few variable region Ig genes and that some somatic process (for example, mutation or recombination) creates a large number.

The chemical nature of receptors on T cells is probably the most controversial issue in cellular immunology at present. The simplest and most logical view, that only antibody can recognize antigen and that all antigen-specific receptors must be Ig, has been challenged by the failure of many investigators to demonstrate Ig directly on the surface of T cells, or to inhibit various T cell responses with anti-Ig sera. Indeed, there is now growing support for the idea that surface com-ponents other than classical immunoglobulin may play an important role in T cell recognition of and/or response to at least some antigens. The principal candidates for such T cell "receptors" are the products of the immune response (Ir) genes that are genetically linked to the chief histocompatibility loci[45]. These Ir genes influence T cell responses to a variety of antigens[46]. The exquisite specificity of T cell responses, which resembles very closely the specificity of antibody and B cell recognition[47], taken together with the various (but still controversial) demonstrations of Ig on T cells (reviewed in ref. 1), makes one reluctant, however, to give up the idea that T cells have Ig receptors. It is possible that T cells (and possibly B cells) have at least two "recognition" systems, one involving Ig and another mediated by Ir gene products, the

general importance of each varying depending on the antigen, the response and/or the subclass of T cell. The putative non-Ig recognition system could be analogous to the primitive recognition of foreignness seen in invertebrates.

Functions of T and B Cells

When an antigen combines with its corresponding receptors on a T or B lymphocyte, one of at least three things can happen to the lymphocyte: first, it may be stimulated to divide and differentiate to become an effector cell in some type of immune response (that is, it is induced to respond immunologically); second, it may become immunologically tolerant or paralysed, so that it will not be able to respond the next time antigen is given; it is not known if such cells are killed or simply inactivated in some way; third, it may be unaffected by the encounter. In addition, if the animal makes an immune response to the antigen, on subsequent exposure to the same antigen, it will usually give a faster, greater and sometimes qualitatively different response. This altered state of immune reactivity to a specific antigen is called immunological memory. It is likely that memory involves both clonal expansion (that is, division of virgin lymphocytes to give an increased number of cells able to respond on second exposure) and differentiation of virgin cells to memory cells[1], but it is unclear whether memory cells are simply retired effector cells, cells at an earlier stage of differentiation than effector cells, or are derived by differentiation along a separate memory pathway.

The "decision" of an individual lymphocyte on encounter with antigen—whether to "turn-on", "turn-off" or ignore—depends largely on the nature and concentration of the antigen, and upon complex interactions with other lymphocytes and with macrophages. Although most immunogens can stimulate both T and B cell responses, some, particularly those with repeating identical determinants and which are poorly catabolized—the so-called "thymus-independent antigens" (for example, pneumococcal polysaccharide, E. coli endotoxin, polyvinylpyrrolidone)—chiefly stimulate B cells (reviewed in ref. 1), whereas others preferentially activate T cells[48]. In general, T cells respond to lower concentrations of antigen than do B cells, and although T cells may be paralysed at very low and very high concentrations of antigen (low and high zones of tolerance respectively) B cells seem to be paralysed only at high antigen concentrations[49]. The way in which the antigen-receptor interaction signals a lymphocyte is unknown, although it probably involves allosteric changes and/or redistribution (for example, aggregation into patches or localization over one pole—cap formation[50]) of the membrane-bound receptors.

The most important differences between T and B cells concern their different functions in immune responses. When B cells are activated by antigen they divide and differentiate into blast cells with abundant endoplasmic reticulum, and some go on to become plasma cells. These cells remain in the lymphoid tissues for the most part and secrete large amounts of antibody which circulates in the blood. Individual antibody-secreting cells can be detected by a variety of techniques, the most common being the plaque-forming cell assay, in which anti-erythrocyte antibody released from single B cells lyses erythrocytes in their immediate environment in the presence of complement. Antibodies, in conjunction with various accessory cells (macrophages, mast cells and basophils, for example) and particular serum enzymes (complement components, for example), are responsible for a variety of hypersensitivity reactions and protective immunity against many pathogenic organisms. In addition, antibody serves to regulate the function of both T and B cells, inhibiting their responses by competing with lymphocyte receptors for the antigenic determinants, diverting antigen from the lymphoid tissues or by forming tolerogenic antibody-antigen complexes[51], and enhancing responses by localizing antigen to appropriate lymphoid tissues or perhaps forming immunogenic antibody-antigen complexes. It is also possible (but not established)

that B cells themselves play a direct part in transporting antigen (perhaps as antigen-antibody ± complement complexes adhering to Fc or complement receptors on B cells) and/or in killing target cells with coated antibody[52].

When T cells are activated by antigen, they proliferate and differentiate to become blast cells, but they do not develop significant amounts of endoplasmic reticulum and do not become antibody-secreting cells. They do, however, secrete a variety of non-antigen-specific factors ("lymphokines") such as migration inhibition factors (MIF), chemotactic factors, cytotoxic factors and mitogenic factors, at least some of which presumably play a role in cell-mediated immune responses, for which T cells are primarily responsible[53]. The precise chemical nature of these factors, the relationship between them, their significance and mechanisms of action are, however, incompletely understood. Cell-mediated immune responses include delayed hypersensitivity, contact sensitivity, rejection of foreign tissues, graft versus host responses (where injected foreign T lymphocytes respond against the antigens of the recipient, often resulting in recipient death) and immunity to various microbes. In all of these responses, T cells enlist the help of macrophages (probably through the secretion of lymphokines). The latter are usually the predominant cells at the site of these reactions[54]. T cells can also be demonstrated to respond to antigen in vitro by dividing, secreting lymphokines, killing target cells, or supporting viral replication (reviewed in ref. 1). Whether T cells themselves can directly kill target cells, or do so only by activating other cells (such as macrophages) is still controversial, although there is increasing evidence that they can become "killer cells" under some circumstances[55].

Although T cells do not themselves secret antibody in the usual sense, it is now known that they play an important role in helping B cells to make antibody responses to most immunogens. Thus, in these responses T cells are referred to as "helper" cells, and B cells as "antibody-forming precursor" cells. The first direct evidence for such T-B cell cooperation was provided in 1966 by the observation that irradiated mice given both thymus cells and bone marrow cells made a far greater antibody response to sheep erythrocytes (SRBC) than recipients of either thymocytes or bone marrow cells alone[56]. Subsequently it was shown that all of the antibody-secreting cells (that is, those making anti-SRBC antibody) in this type of experiment came from the bone marrow inoculum[57]. Independent studies with chemically defined antigens showed that T-B cell cooperation in antibody responses involved T cells responding to one antigenic determinant on an immunogen and helping B cells to respond to different determinants on the same immunogen[58]. Although it is clear that cooperation is usually mediated by such an "antigen bridge" between T cell and B cell receptors, it is still uncertain whether the bridge is between T and B cells themselves, or between shed T cell receptors (perhaps taken up on the surface of macrophages) and B cells, and whether the bridge serves to "present" antigen to B cells in a particularly immunogenic form (concentrated and multivalent, for example) or to bring B cells close to T cells or a third party cell (such as macrophage) so that a non-specific, short-range factor (for example, chemical mediator or membrane-membrane interaction) can operate between them (Fig. 2). Although it has been shown that T cells can secrete non-specific factors which can enhance B cell responses[59], their role in normal T-B cell cooperation is still uncertain. There is recent evidence that, in some in vitro responses at least, cooperation may involve the release by T cells of antigen-specific IgM-like factors (? receptors) complexed with antigen, which are subsequently taken up on macrophages[60].

There are antigens ("thymus-independent antigens") which seem to be able to stimulate at least some B cell clones to secrete IgM antibody without the help of T cells (reviewed in ref. 1), suggesting that T-B cell collaboration is not always essential for antibody production. Nonetheless, the discovery
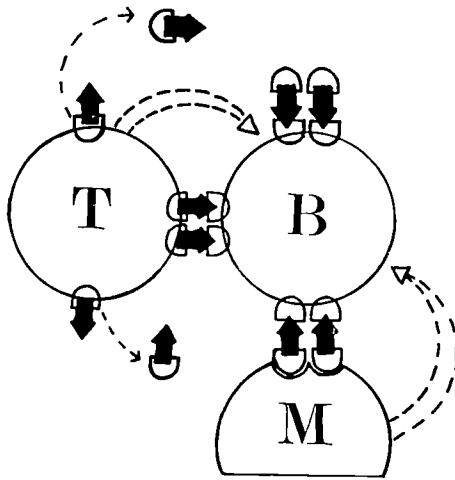
Fig. 2 Possible mechanisms of T-B cell collaboration in humoral antibody responses. The "antigen bridge" (→) between T and B cell receptors could serve to: (i) present antigen to B cells on the surface of T cells or as a matrix of released T cell receptors complexed with antigen, either free or on the surface of third party cells such as macrophages, or (ii) bring B cells together with T cells or a third party cell so that a short-range factor can operate between them.

that T cells cooperate with B cells in humoral immunity has been an important advance and has explained the previous paradox of impaired antibody responses in T cell deficient animals. There is recent indirect evidence that T cells can inhibit B cell activity as well as enhance it[61], and that they can enhance[62] and inhibit[63] the functioning of other T cells. It is not known if these interactions involve antigen bridging between the receptors of the interacting cells. Taken together with the enhancing and inhibiting effects of secreted antibody on both T and B cell functions, a picture is emerging of a highly complex and finely controlled immune system, with each type of cell and response modulating the others.

Way Ahead

With the recognition that there are two distinct classes of lymphocytes with different origins, properties and immunological functions which modulate each other's activities, the door has opened to a new era of immunology. The resulting insight into the functioning of the immune system in health and disease has paved the way for rational attempts to manipulate selectively the different cell types and their various responses for the benefit of patients with infection, autoimmune disease, cancer, immune deficiency states, and organ grafts. And present day immunology provides a number of readily accessible models and powerful tools for studying a variety of biological problems, including differentiation, genetic control, cell interactions, and membrane receptor-ligand interactions.

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Multiple Universes

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Professor Gold considers the properties of a closed or nearly closed universe in which there are substantial variations of mean density on a large scale, so that close "sub-universes" could exist within it.

MOST cosmological discussion assumes that the Universe, although locally obviously non-uniform in its content, tends to uniformity on a large scale. In particular it is assumed that on the scale of the "radius of the Universe" R_0 (defined by setting $V=c$ in the Hubble expansion law $D=V/H$, where V is the velocity of objects observed at the distance D and H is Hubble's constant) sufficient uniformity is reached for the principal conclusions of geometry to depend on a single large scale radius of curvature only.

Modern observations of distant parts of the Universe do not make a clear case for such uniformity. A number of seemingly strange non-uniformities have been pointed out, such as super-clusters of galaxies[1] or patterns of quasars[2,3]. No observations seem to demonstrate that a smooth distribution of matter does indeed exist on the largest, cosmological scale of distances.

Sandage et al.[4] have presented evidence that no large dynamical effects can be attributed to inhomogeneous mass distributions on the intermediate distance scale accessible by optical observations of ordinary galaxies. On the other hand, the evidence of quasars, which refers to a much larger distance scale if one assumes that universal expansion is the chief cause of their redshifts, is still entirely confusing (see, for example, Rees[5]). It is therefore appropriate to consider the consequences of the existence of non-uniformity on the large scale also. Time constants for gravitational contraction of matter unresisted by physical pressure are given by $(G\rho)^{-\frac{1}{2}}$ (where G is the gravitational constant and ρ is the density of the contracting region) and are independent of the scale. Thus a large region can collapse on this basis just as fast as a small one.

The condition for closure of our Universe $\dfrac{2GM_0}{R_0}=c^2$ can be written as

$$\frac{8\pi G R^2{}_0 \rho_0}{3}=c^2$$

or, leaving out all small numerical factors, as

$$(G\rho_0)^{-\frac{1}{2}}=\frac{R_0}{c}$$

$(G\rho_0)^{-\frac{1}{2}}$ is the time constant for gravitational collapse for a region of any scale but of density equal to the mean, and R_0/c is the "age of the Universe" defined by the expansion. Apart from small factors which are different in different cosmological models the two times are the same. Thus a universe of such

density that it is closed or nearly closed is one in which there has been enough time available to generate great density variations on any scale. The general expansion and physical pressures would oppose the growth of such inhomogeneities. The effect of expansion as a stabilizing influence is different in different cosmological models; physical pressure is always least important on the largest scale. There is no general argument that the large scales should have been protected from the growth of gravitational condensations when it is clear that smaller scales were not.

The mass density existing in large spaces is observationally a very poorly known quantity. Obviously the assumption that all mass is in stars that are luminous is a poor one with no real justification. Even the assumptions that mass is chiefly in galaxies, and that galaxies emit light in proportion to their mass, are very questionable. The dynamical estimates seem to lead in each case to a large amount of unseen mass; for example the dispersion of velocities seen in clusters of galaxies is very much greater than the values that would be given by the virial theorem for masses estimated by means of the assumptions mentioned above.

Unseen mass can exist in several forms that would have escaped present means of detection. Ionized hydrogen can occur in comparatively large amounts in intergalactic space; cold disks of rotating condensed matter may be as common as stars; black holes of stellar masses may also be common; gas galaxies, in which star formation has not proceeded very far, may be members of clusters. Thus the mean density in the
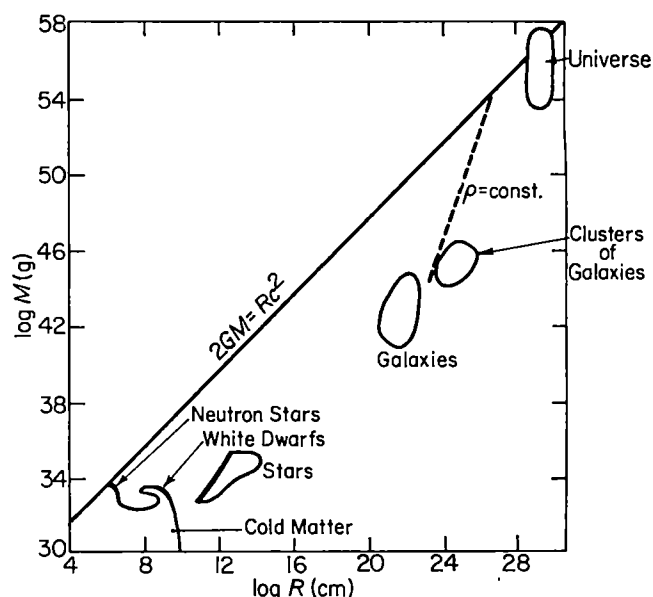
Fig. 1 Radius (R) against mass (M) for objects in the Universe. The lower right half contains known objects; the diagonal line represents the gravitational singularity. - - -, Constant density line showing where the largest clusterings of matter might be situated, up to the singularity.

Universe is at least 10^{-33} g cm^{-3}, as judged from the starlight emitted by galaxies, but it may be more. A value in the vicinity of 10^{-30} g cm^{-3} is possible, and that, for modern estimates of the expansion constant, would make the Universe closed within the radius R_0; in fact, most cosmological discussions assume a density of this order.

It is of interest then to consider the geometrical properties of a universe which is closed or nearly closed within R_0, but in which there are substantial variations in mean density even on a scale comparable with R_0. In such a universe subunits may have the mass necessary to make them closed in turn. The requirement for that would be that their density is greater than the mean by a factor $\left(\dfrac{R_0}{R}\right)^2$, where R $(< R_0)$ is the radius of such a region. Therefore progressively smaller irregularities of density are sufficient to cause closed subunits as one approaches the scale of the "radius of the universe" R_0.

Black holes of stellar or galactic masses have been discussed as being possible members of our Universe. But there the factor $\left(\dfrac{R_0}{R}\right)^2$ is very large; high densities have to have been built up and the complex physical processes leading to such contractions of matter need to be discussed. On a large scale the densities implied by closure are low, and not of a kind that would be associated with any particular set of physical processes, but merely with the statistics of the large scale distribution of matter. If, as larger and larger scales are examined, one again encounters excursions of the density from the cosmological mean approaching the factor $\left(\dfrac{R_0}{R}\right)^2$, where R is the scale examined, then one must suspect that singularities on such a scale may also exist in our Universe. Clusters of galaxies have densities which, if estimated on the basis of the velocity dispersion and the virial theorem, are indeed greater than that necessary to generate singularities on a scale of $\frac{1}{10}R_0$; thus if density variations of this or even somewhat smaller magnitudes persist to large scales, they would be singularities and therefore would not be seen as large clusters.

Such objects would not be readily identifiable. In our geometrical picture they would appear as points, or, if insufficient time has been available for the completion of the distortion, whose last phase is infinitely slow in our time frame, they would appear as very small areas of great redshift. There is no reason for associating any great luminosity with them. Internally they may be universes smaller than ours only by a small factor. The particular space open to us may in turn be a closed subunit in another slightly larger universe. Indeed, if we are embedded in a space having more than a certain dispersion of density, we would have to regard it as coincidental if our accessible space, our Universe, was the first (in ascending order of size) that possessed the density for closure. If not, then other "universes" would be part of ours, just as ours might be a component of a larger one. There would be a system of "nesting universes" in which each is perhaps only slightly smaller than the one in which it nests.

There is, of course, no theoretical constraint preventing our discovery of massive singularities in our Universe; but, within the understanding of the movement of information in relativity theory, we would have no access to any information about any larger scale than that of our closed space.

Can present observations tell us whether large gravitational singularities exist in our Universe? The geometrical properties of our Universe would of course be severely affected if most of its mass were in the form of a small number of singularities. As the "seen" mass is only approximately 10^{-3} of that necessary for closure, these may, in the most extreme case, be as much as 10^3 times the "seen" mass in the form of large singularities. Space would then be extremely uneven both in directional and in temporal properties. Distant light sources would be seen in directions severely distorted by space curvature and the local density of any class of objects is then quite different from the density determined from our vantage point, without allowance for this distortion. Equally the frequency shifts of spectral lines would be severely changed by the gravitational redshift, and different for different large regions of observations.

Gravitational redshifts seemed inadequate as an explanation for observed redshifts when only mass concentrations on a galactic scale were assumed and any gradient of potential over the luminous region would widen the lines beyond the observed amount. There is no such difficulty if one assumes that there are large, cosmic scale singularities. In their vicinity galaxies, and even large clusters of galaxies, can be accommodated in a gravitational potential of very slight gradient only, but of a value very different from that in our locality; we would therefore observe such galaxies with a spectral shift due to this difference in gravitational potential, superimposed on any Doppler shift due to expansion. The observation of blueshifts would then be a possibility in principle, for we could observe galaxies in lower gravitational potentials than that of our neighbourhood. The general expansion may, however, make such an effect very improbable and result in the observation of redshifts only. The possibility of regional effects does, then, exist. There may be significant variations in the number per unit solid angle of objects seen within a certain range of values of the redshift. Such effects have been suspected[2,3], but their statistical significance is still not clear.

The universal background radiation is not expected to show any anisotropies as a result of distortions of space geometry. A uniform surface brightness remains uniform and unchanged when viewed through space refracting the rays in any manner whatever (this of course is required to avoid an infringement of the Second Law of Thermodynamics). Thus if the background radiation was set up initially as a uniform brightness, the subsequent development of gravitational distortions of space would not have any effect. The absorption of radiation by a singularity is an effect that could introduce an observable anisotropy, but the time scale of the development of this effect is not clear.

The observation of the apparent strengths of radio sources, without knowledge of distance or redshift, is concerned with the greatest number of objects and may therefore be most sensitive for the detection of severe space distortions. But here also there are severe limitations. A uniform distribution of sources in Euclidian space results in the relation $N = S^{-3/2}$ where N is the number of sources seen of an apparent strength exceeding S. The form of this relation is maintained when the region is viewed through a convergent or divergent lens, but the numbers are changed, although not very critically. Thus the isotropy of this type of observation can place a limit on space distortions, but only if it is certain that the contribution in each sample is dominated by intrinsically strong and distant sources rather than by intrinsically faint but nearer ones. The indication that this is so is derived from the appearance of a slightly steeper law in the relation between N and S than that for uniform Euclidian space, but observers are not yet in agreement as to the reality of this effect. Nevertheless it is clear that modern observations by radio and optical means will be able to give a limit to the extent of space distortions occurring in our Universe, and therefore it will be possible to answer the question whether there are other universes nesting within our observable space.

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Intrusion, Extrusion and Metamorphism at Constructive Margins: Evidence from the Troodos Massif, Cyprus

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Evidence from the Troodos Massif for the origin of the ocean floor is discussed and a detailed model formulated.

RECENT proposals that the Troodos massif of Cyprus represents a subaerially exposed slice of oceanic lithosphere[1-4] have received wide acceptance. In some of these works[2,3] the principal units of the massif have been correlated with seismic layers 2, 3 and 4 of the ocean floor (Fig. 1).
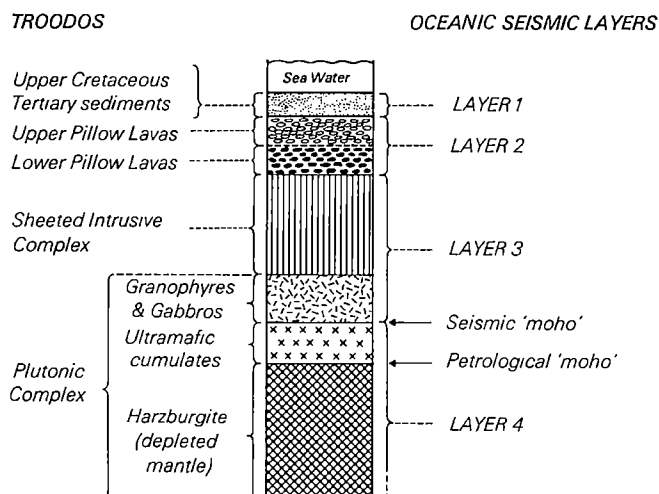
Fig. 1 Correlation between Troodos units and oceanic seismic layers.

The significance of the processes that operated in the Troodos magma chamber in elucidating those beneath the axes of oceanic rises has already been discussed[3,4]; here we discuss the genesis and metamorphism of the Sheeted Intrusive Complex and the overlying Pillow Lava Series which, in oceanic terms, are seismic layers 2 and the upper part of 3.

During the past two decades numerous attempts have been made to subdivide realistically this intrusive/extrusive sequence[5-10]. It is reasonable therefore to start with the currently accepted model which is based on primary and secondary petrological differences and on intrusive/extrusive abundance ratios.

Since detailed petrographic and analytical data became available, it has been recognized that there is a primary difference between the two divisions of the Pillow Lava Series (see Fig. 1). Perhaps the most convincing evidence is the abundance of olivine in the upper division and its absence in the oversaturated lavas of the lower group. This, coupled with the varying abundance of dykes, low in the upper and high in the lower division, were the main factors on which the Upper Pillow Lava/Lower Pillow Lava boundary was drawn. But at many localities these various criteria do not coincide nor are they sufficiently obvious to allow an accurate, unique boundary to be drawn. Nevertheless, most workers were in agreement that there were two divisions to the Pillow Lava Series.

Divisions of Pillow Lava Series

Towards the base of the Pillow Lava Series dykes become abundant and commonly form as much as 60% of the outcrop although they maintain the sinuous form common to this division of the massif. Then, within a short lateral distance, they give way to the Sheeted Intrusive Complex with its high dyke density (90%) and planar dyke form. The contact between the two divisions commonly coincides with a marked increase in local topographic relief. The abruptness of this change led some[1,8] to propose that it represents an unconformity, whereas others[3,6,7,9] preferred a gradation, over a short distance, between the two units. At

Table 1 Distinguishing Features on which the Geological Subdivision of the Troodos Massif was Proposed

Sediments	
Upper Pillow Lavas	Generally undersaturated, often olivine-bearing, basalts with more basic varieties (limburgites and picrites) occurring at the top of the sequence. Dykes form less than 10% by volume, absence of silica and celadonite, calcite and analcime common
Boundary	Varying laterally from unconformity to transitional
Lower Pillow Lavas	Mainly oversaturated basalts, often intensely silicified, celadonite common. Dykes, sills and massive flows forming between 30-60% of the outcrop
Boundary	Interpreted as unconformity and gradational
Sheeted Intrusive Complex	Hard, indurated meta-basalts forming an intense dyke swarm of sheeted aspect. Pillow Lava Screens form 10% at most of the outcrop on the upper surface, diminish to zero with depth.
Troodos Plutonic Complex	See refs. 3, 4

the top of the Sheeted Intrusive Complex pillow lavas occur as narrow, elongate screens forming, at most, 10% of the outcrop. With increasing depth they become less abundant until the 100% dyke form of the Sheeted Intrusive Complex is evident.

The distinguishing features on which these divisions were erected are shown in Table 1.

The Troodos structure described above fits well with the seismic data for the oceanic lithosphere. But several workers[11-14] have noted the metamorphic imprint on basaltic rocks dredged from the deep ocean floor. With this in mind, one of us (J. D. S.) began a study of the north side of the Troodos massif where excellent exposures of meta-basalts are abundant. We present here the preliminary findings, for they support the seafloor spreading concept, offer an alternative explanation for an oceanic seismic discontinuity and allow the deduction of the metamorphic processes at a constructive margin.

The metamorphic minerals and their distribution within the massif indicate that the previously erected subdivision of the Pillow Lava Series into upper and lower units is

Lavas to be easily identified. This evidence, coupled with the primary morphology and attitude of the lavas, makes it possible to delineate a continuous unconformity between the Upper and Lower Pillow Lavas along the northern flank of the massif. But lavas of the upper division are commonly found directly overlying rocks of the greenschist facies, which supports the proposal that the Upper Pillow Lavas rest unconformably on all underlying formations. A period of extensive sub-aqueous erosion is suggested because: Upper Pillow Lavas rest directly on greenschist facies rocks (see above); neither unmetamorphosed nor submarine weathered basalts occur at the top of the Lower Pillow Lavas which is within a homogeneous zeolite facies; vertical feeder dykes are cut off at the contact; erosional conglomerates are associated with sedimentary sulphide deposits which formed in depressions on the Lower Pillow Lava surface[16]; and unequivocal evidence for widespread submarine erosion occurs on the south side of the massif where extensive sedimentary sequences overlie greenschist facies rocks and are, in turn, overlain by Pillow Lavas (K. Simonian, personal communication).

Table 2 Metamorphic Phases and their Distribution within the Troodos Massif
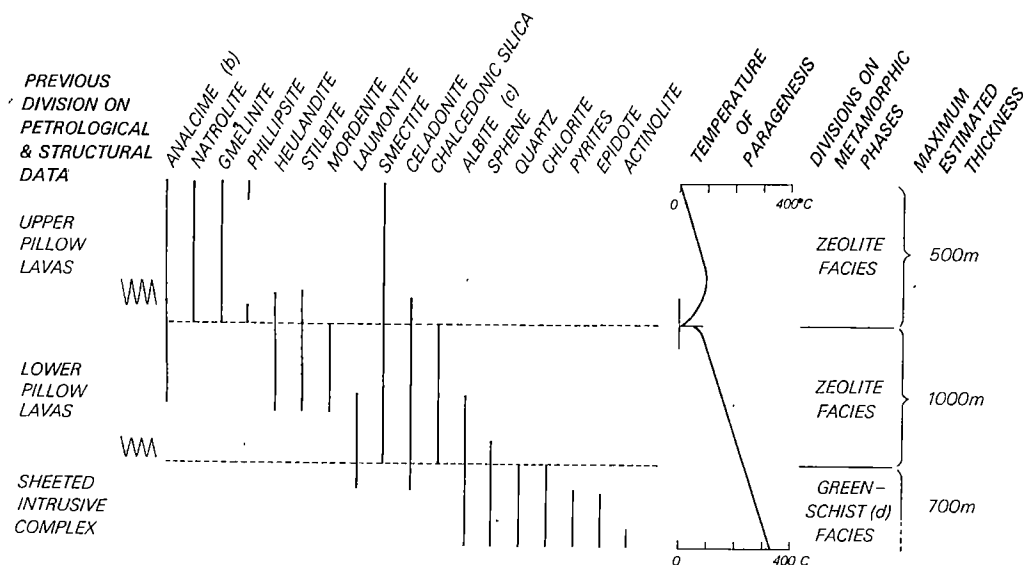
Temperatures of paragenesis when related to maximum thicknesses of facies suggest a minimum thermal gradient of 150° C km^{-1}. a, Chabasite, a rare zeolite on Troodos, has been recorded at two localities in the upper division and one in the lower division of the Pillow Lava Series; b, analcime occurs as macroscopic, commohly amygdaloidal, crystals in the upper unit but only in the ground mass of the Lower Pillow Lavas; c, the anorthite molecule is metastable within the albite stability field near its upper temperature phase boundary; d, we retain the term greenschist but appreciate, as others have done[12-14], that it is inappropriate in an oceanic environment.

valid. As previously suggested[3], however, only the lower division is genetically related to the underlying Sheeted Intrusive Complex. The distribution and temperature parameters of these secondary phases within the three divisions listed in Table 1 are shown in Table 2.

The Upper Pillow Lavas are characterized by the presence of the zeolites, natrolite and gmelinite, which are unique to this division. Phillipsite occurs only at the top and bottom of the sequence and, because it is a zeolite typical of a low temperature (0° C) environment[15], this suggests that these lavas were poured out over a cold oceanic crust and produced their own perched thermal gradient. This proposal is entirely in keeping with the view, based on petrological data, that the Upper Pillow Lavas are genetically distinct from the underlying rocks.

Evidence for Sub-aqueous Erosion

The characteristic zeolite assemblage (see Table 2), together with widespread silicification, allow the Lower Pillow

Perhaps the most convincing evidence for this strong erosional episode is that it produced such a marked and irregular topography that inliers of the Sheeted Intrusive Complex and Lower Pillow Lavas occur as "islands" completely surrounded by a "sea" of Upper Pillow Lavas.

Metamorphic Boundary

On Troodos, the zeolite facies/greenschist facies boundary is everywhere transitional and nowhere has an intervening prehnite-pumpellyite facies, characteristic of burial metamorphic sequences[17-19], been found. The metamorphic boundary is completely gradational over a vertical distance of between 10 and 20 m. When the vertical exposure is sufficient, any single dyke at the contact shows a transition from a soft, grey-brown rock in the zeolite facies to a hard, light-green-blue rock in the greenschist facies. There is no evidence that this metamorphic contact coincides with any primary structure such as a rapidly changing dyke density; the boundary seems to be entirely independent of the intrusive/extrusive ratio. Thus, in terms of the existing
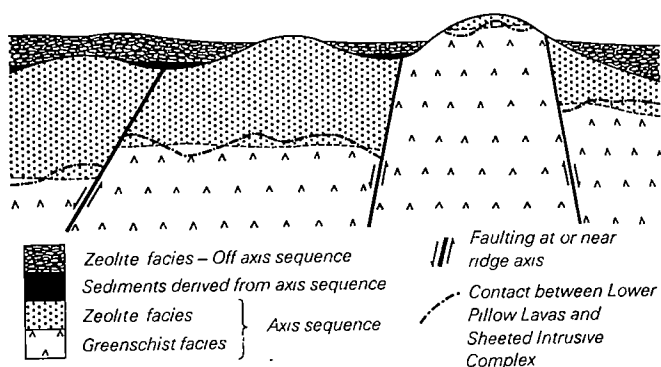
Fig. 2 Schematic cross section showing the relationship of metamorphic facies to units delimited on structural and petrological data.

subdivisions, the metamorphic contact can occur either within the Lower Pillow Lavas or the Sheeted Intrusive Complex. The relation of metamorphic to structural and petrological units is shown diagrammatically in Fig. 2.

Microscopic studies reveal that the metamorphic boundary involves the replacement by quartz and a chlorite mineral of fixed composition (pycnochlorite: $Mg_{2.35} Fe^{2+}_{2.6} Al_{1.05}$ $(Si_{2.95} Al_{1.05}) O_{10}(OH)_8$ identified from optical data[20]) of the smectite, tentatively identified as nontronite, so common in the zeolite facies above. The incoming of quartz imparts a hardness to the greenschist facies rocks. Below the facies boundary, epidote, and then actinolite, appear as essential phases with increasing depth.

Experimental data[21,22] show that for these metamorphic minerals increasing pressure affects, only slightly, the temperature at which the minerals are stable. Therefore temperature is the prime controlling factor and from the temperature of paragenesis of these minerals estimated predominantly from borehole data in present day active metamorphic regions[23,24], a thermal gradient of 150° C km^{-1} for the Lower Pillow Lavas and Sheeted Intrusive Complex can be deduced. The lowest temperatures of mineral paragenesis and the maximum thicknesses of rock sequences were taken in calculating this thermal gradient. 150° C km^{-1} is therefore a conservative estimate; nevertheless, such a thermal gradient would preclude the existence of a prehnite-pumpellyite facies; this agrees with the field data.

In relating the Troodos evidence to processes at constructive margins, it is evident that only the Sheeted Intrusive Complex and the genetically related Lower Pillow Lavas are, as previously suggested[3], the products of spreading axis processes. The unrelated Upper Pillow Lavas can be best explained as due to off-axis activity, not only after the two lower units had been formed at the constructive margin, but after they had had the metamorphic regime imprinted upon them. Hereafter we refer to the Sheeted Intrusive Complex and the Lower Pillow Lavas collectively as the Axis Sequence and propose that it is a gradational sequence resulting from the injection of dykes and effusion of lavas on or near a ridge axis. As well as fitting with the Troodos data, this proposal is in keeping with experimental evidence[25,26] which indicates that oversaturated basalts such as these could well equilibrate in a high level magma chamber beneath the ridge axis[4,27].

Magmatic and Metamorphic Processes

We follow Cann[11] in envisaging that the axis magma is injected along vertical fissures at or near the ridge axis. We further suggest that the planar structure of the dykes within the Sheeted Intrusive Complex is entirely because the host rock consists, almost entirely, of pre-existing, near-vertical dykes. But when such a dyke enters the homogeneous extrusive pile of overlying pillow lavas it has no structural

restraints imposed upon it and finds its way towards the surface along the easiest line of access which is commonly sinuous. This transition from the planar structure in the Sheeted Complex to the overlying pillow lavas with their sinuous dykes was used by previous workers[5-10] to define the boundary between the two units. Although the evidence presented here indicates that the boundary has no petrogenetic significance, we are still at a loss to explain the sometimes extremely rapid upward change in dyke abundance.

Cann's model[11] requires a thermal gradient of some 500° C km^{-1} at ridge axes; indeed, all active oceanic ridges are characterized by high heat flow values. Heat flow profiles across oceanic ridges[27,28] and thermal models derived therefrom[29,30] all suggest that a thermal gradient of 150° C km^{-1} must be well within 100 km of the ridge axis—the wide scatter of heat flow values over the ridges precludes any more accurate predictions. With the Troodos evidence in mind, we suggest metamorphism is imprinted upon the oceanic lithosphere within 100 km of the spreading axis and will take place at a constant distance from the ridge throughout the spreading process. So at this point the metamorphic facies will be produced and the near-horizontal disposition of the greenschist/zeolite facies boundary established as seafloor spreading continues.

We have already noted the variance in physical properties between the rocks of the greenschist and zeolite facies on Troodos. In particular, the presence of quartz in the greenschist facies gives it a rigidity that is distinctly greater than that of the zeolite facies above. This has a marked effect on the seismic velocities, as shown by recent shortline refraction experiments at the Troodos outcrop[31] when velocities averaging 3.2 km s^{-1} were obtained for what are now recognized as the zeolite facies rocks and 4.9 km s^{-1} for those of the greenschist facies. So, although these velocities are low when compared with those from the layers of the oceanic lithosphere, this can be accounted for by the porosity in the near surface rocks of Troodos. Further, it may be significant that the difference in P wave velocities for oceanic layers 2 and 3 is 1.6 km s^{-1}, virtually identical for that between the two metamorphic facies on Troodos. The greenschist/zeolite facies boundary, marking as it does a distinct rigidity difference, could represent the seismic discontinuity between oceanic layers 2 and 3. We are, however, aware that the greenschist/amphibolite facies boundary has been suggested as the metamorphic contact most likely to represent the layer 2-layer 3 seismic discontinuity[32]. The greenschist/amphibolite facies boundary, if present on Troodos must be studied in more detail and velocity of sound in jacketed samples under confining pressure of rocks from the various facies determined, before any more realistic statement can be made concerning the seismic significance of the zeolite/greenschist facies boundary.

The dominant basaltic rocks of the deep ocean basins are quartz and olivine normative tholeiites. So far as we are aware, although alkali basalts have been found[33], more basic lavas such as limburgites and picrites, recorded from the Upper Pillow Lavas of Troodos, have not been dredged from the oceanic rises. We have already presented evidence that the Upper Pillow Lavas of Cyprus are a manifestation of off-axis magmatic activity. The simplest explanation would be that the Upper Pillow Lavas are analogous to the numerous sea-mounts and volcanic islands that embellish the present day oceanic crust away from the ridge axis and are probably produced by thermal plumes rising from the thermally unstable lithosphere/asthenosphere interface. Certainly their undersaturated nature is in keeping with such a proposal as oceanic volcanic island lavas seem to become progressively undersaturated in silica with increasing distance from the ridge axis[28]. But the Upper Pillow Lavas are nowhere more than 500 m thick, show no gross morphological features indicating a localized lava pile, have no extensive underlying

sedimentary unit and related intrusives are structurally concordant with those in the underlying axis sequence rather than having a radial pattern characteristic of oceanic volcanic islands. It seems likely therefore that the Upper Pillow Lavas were erupted on an oceanic rise, relatively close to a spreading axis, before a sedimentary sequence had time to develop and that the products of this activity were nowhere so thick as to allow a high level chamber to develop and produce its· characteristic radial fracture pattern.

Whatever the genesis of the off-axis sequence, we propose that, on Troodos, the underlying volcanic rocks represent the products of constructive margin processes, that the rocks were metamorphosed to greenschist and zeolite facies within 100 km of the axis and were subsequently subjected to block faulting and intense local submarine erosion as seafloor spreading continued. The production of this uneven topography near the axis allowed the accumulation of conglomeratic sediments, sedimentary sulphide deposits and later lavas in the bathymetric depressions. Seismic and petrological evidence from the oceanic lithosphere suggests that this model, in part at least, is applicable to the present cycle of seafloor spreading.

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A Factor Preventing the Development of Lung Metastases in Rats with Sarcomas

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An immunologically specific factor circulating in lymph and blood prevents the occurrence of lung metastases in rats with sarcomas growing in the leg. Removal of thoracic duct lymph causes such tumours to metastasize to the lung. This is due to the removal of a plasma factor and not of lymphocytes.

THE capacity of rats bearing sarcomas, induced by carcinogenic hydrocarbons, to reject a second subcutaneous challenge with cells from the same tumour is much less than that of rats in which the initial tumour has been surgically removed[1]. The growing tumour has also been shown to prevent the discharge of cytotoxic immunoblasts from the draining node probably as a result of flooding the draining node with tumour-specific antigen[2]. While such tumour-bearing animals show low immunological resistance to tumours at intramuscular sites and impairment of the function of the draining node, yet lung metastases arising from intramuscular tumours are uncommon. We have several established lines of chemically induced sarcomas which when implanted intramuscularly into normal syngeneic rats never metastasize to the lung but which readily give rise to lung tumours following intravenous injections (that is, the cells can grow in the lung but do not do so in tumour-bearing animals). We set out to test the hypothesis that the tumour-bearing rat elaborates a circulating humoral factor which protects against bloodborne tumour cells lodged in the lung and which is relatively ineffective in preventing the growth of intramuscularly inoculated tumour cells.

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Table 1 Effect of Serum and Lymph from Tumour-bearing Rats on Growth in the Lung of Intravenously Injected MC-I Rat Sarcoma Cells

	10^6 MC-I cells [†] injected intravenously		2×10^4 MC-I cells [†] injected intramuscularly	
Pretreatment [*]	No. of rats with lung tumours	Average No. of tumour nodules in lung per rat [‡]	No. of animals with tumours	Average weight of tumour (g)
(1) None	10 out of 10	12.1 (2–31)	—	—
(2) Serum from rats with MC-I sarcoma	5 out of 10	2.6 (0–8)	5 out of 5	5.8
(3) Serum from normal rats	9 out of 10	10.1 (0–21)	4 out of 5	7.8
(4) Serum from rats with antigenically unrelated MC-III sarcoma	5 out of 5	8.6 (2–25)	—	—
(5) Lymph plasma from normal rats	10 out of 10	7.9 (1–14)	—	—
(6) Lymph plasma from rats with MC-I sarcoma	6 out of 10	2.7 (0–10)	—	—

According to the Mann-Whitney nonparametric test the difference in the number of lung tumour nodules between group 2 and group 1, 3 or 4 and between groups 2 and 5 is significant at $P<0.01$.

[*] Serum (6 ml.) was injected intraperitoneally 4 h before inoculation of tumour cells Thoracic duct lymph (150 ml.) free of cells was injected intraperitoneally in five aliquots of 30 ml. over a period of 24 h, one day before challenge with tumour cells. Serum and lymph were collected from rats that had been inoculated with a mechanically dispersed suspension of tumour 8 days previously and all of which had a growing tumour of between 0.5–1 cm diameter.

[†] Prepared by trypsin digestion of a solid tumour. Rats were killed 26 days later and tumours weighed.

[‡] Values in parentheses are the range of values.

In the first series of experiments the possibility of transferring resistance to tumour challenge with the serum or lymph plasma from tumour-bearing rats was examined and Table 1 shows that, following injection of such serum, rats were resistant to an intravenous challenge (that is, the number of lung tumours was reduced) but the growth of tumour cells injected intramuscularly was unaffected. The tumour used was the MC-I sarcoma which had been induced with methylcholanthrene and is highly antigenic; no intramuscularly growing MC-I tumour has been found to metastasize spontaneously to the lung. That this protection by tumour-bearing serum is immunologically specific is indicated by the failure of serum from rats bearing the immunologically unrelated chemically induced sarcoma, MC-III, to protect against MC-I tumour cells given intravenously. The failure to transfer resistance to an intramuscular challenge passively with serum is, of course, in line with many experiments in the field of transplantation immunity, originating with the classical studies of Billingham et al.[3]. Passive transfer of resistance to intravenous challenge has, however, been observed with leukaemias[4].

This experiment encouraged us to explore the possible role of a circulating factor in preventing spontaneous lung metastases arising from sarcomas growing in the legs of rats

and which presumably shed tumour cells into the blood. We chose to approach this by cannulating the thoracic duct of rats with established sarcomas growing in the leg, and draining the thoracic duct lymph continuously for six days. After this, the leg with the tumour was amputated; the rats were later killed and the weight of their lung tumours recorded. A number of different chemically induced sarcomas were examined and some, but not all, were found to develop lung metastases following prolonged draining of the thoracic duct. In general, highly antigenic tumours, like the MC-I, could not be induced to metastasize. We studied the mechanism of the induction of lung metastases by removal of thoracic duct lymph with a benzpyrene-induced sarcoma, referred to as "the HSH sarcoma" in its forty-seventh transplant generation. This tumour showed typical individually specific antigenicity and after immunization syngeneic rats were capable of rejecting an intramuscular challenge of 10^5 tumour cells. After removal of thoracic duct lymph from rats with HSH tumours in the leg, lung metastases occurred in every animal compared to an incidence of 20% in rats that had been operated upon but from which lymph had not been drained (Table 2).

The effect of prolonged draining of the thoracic duct is to deplete the pool of circulating lymphocytes so that the

Table 2 Effect of Continuous Removal of Thoracic Duct Lymph from Rats bearing an HSH Sarcoma in the Leg on the Development of Lung Metastases

	Series 1 (thoracic duct drained in rats with 11-day tumour)		Series 2 (thoracic duct drained in rats with 18-day tumour)	
Treatment	No. of rats with lung tumours	Average weight of lung tumours (g)	No. of rats with lung tumours	Average weight of lung tumours (g)
None	0 out of 4	—	0 out of 5	—
"Sham" thoracic duct cannulation [*]	2 out of 5	0.1	2 out of 4	0.2
Thoracic duct drained	4 out of 4	4.6	5 out of 5	3.0
Thoracic duct drained, lymphocytes returned [†]	5 out of 5	1.8	4 out of 4	2.7
Thoracic duct drained, serum from rats with HSH tumour given [‡]	0 out of 4	—	1 out of 4	0.1
Thoracic duct drained, serum from normal rats given [‡]	4 out of 4	2.4	4 out of 4	3.4

The tumour was implanted in leg on day 1, the thoracic duct drained from day 11–16 (series 1) or day 18–24 (series 2). The tumour was amputated immediately after completion of draining thoracic duct and the animal killed on day 61 (series 1) or day 66 (series 2).

[*] Immediately after cannulation duct was tied off.

[†] Washed thoracic duct lymphocytes (5×10^8) from tumour-bearing rats were injected intravenously daily during the period of thoracic duct draining.

[‡] Serum (4 ml.) from rats bearing an 8-day-old HSH tumour (or from normal rats) was injected intraperitoneally every 12 h during the period of thoracic duct draining.

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rats cannot mount a primary immune response[5]. Immunological memory is not abolished, however, and after thoracic duct draining rats retain the capacity to reject in a "second set" manner skin to which they had previously been sensitized[6]. But circulating humoral factors are also removed with the lymph and the levels of immunoglobulins in the blood fall sharply after two days of continuous draining[7]. The experiments summarized in Table 2 indicate that it is the loss of a circulating factor and not of lymphocytes which is responsible for the occurrence of lung metastases following removal of the thoracic duct lymph. The incidence of lung metastases in drained animals was not significantly lowered when washed lymphocytes from the thoracic duct lymph of the same tumour-bearing animals were continuously returned by intravenous injection. That the re-injected lymphocytes rejoined the circulating pool—that is, that they were not so damaged as to be removed from the circulation by the reticulo-endothelial system—is shown (Fig. 1) by the raised
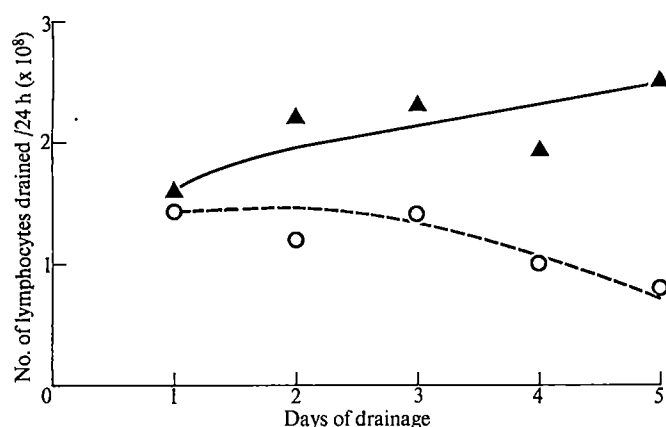
Fig. 1 The effect of returning washed lymphocytes to rats from which thoracic duct lymph has been drained continuously for 5 days. The lymphocytes were collected over 24 h periods at 0° C, washed and returned intravenously (each curve represents the average value from three rats). ▲, Rats with lymphocytes restored; ○, rats with lymphocytes removed. Each point represents the average of three animals.

level of lymphocytes in the lymph of rats which received their lymphocytes back. The direct corollary of this experiment, namely to determine the effect on the incidence of lung metastases of returning the lymph plasma during the period of draining, is technically difficult because of the large volume of lymph removed (that is, up to 150 ml. in each rat per 24 h) and because constituents in the lymph become toxic probably because of autoxidation. Macromolecules present in the thoracic duct lymph accumulate in the blood, however, and consequently another group of rats in the experiments shown in Table 2 received repeated injections of serum collected from a large group of HSH tumour-bearing rats while undergoing removal of thoracic duct lymph over a period of six days. The results clearly show that serum from tumour-bearing animals, but not serum from control rats, prevents the development of lung metastases induced by removal of thoracic duct lymph in spite of the fact that these rats were depleted in circulating lymphocytes.

The active serum factor demonstrated in these experiments is probably produced by circulating lymphocytes, or a cell derived from them, present in tumour-bearing animals because resistance to an intravenous tumour challenge can be transferred with thoracic duct lymphocytes from rats with small tumours (Table 3). As in the case of passive serum transfer, protection was conferred in an immunologically specific way. This experiment is not in conflict with the finding that the return of washed lymphocytes to rats under-

going continuous removal of thoracic duct lymph does not restore the capacity of the rat to prevent the growth of lung metastases. In this last situation, the putative circulating factor even if made by the lymphocytes that have been returned will be lost immediately in the lymph plasma as drainage continues.

Table 3 Effect of Injection of Thoracic Duct Lymphocytes obtained from Rats with a Growing MC-I Tumour on growth in the Lung of Intravenously Injected MC-1 Rat Sarcoma Cells

Pretreatment *	No. of rats with lung tumours	Average No. of tumour nodules in lung per rat †
(1) None	8 out of 8	39.5 (4–58)
(2) Thoracic duct lymphocytes from rats with a growing MC-I tumour	7 out of 8	3 (0 8)
(3) Thoracic duct lymphocytes from rats with antigenically unrelated MC-III tumour	8 out of 8	23.8 (1–58)
(4) Thoracic duct lymphocytes from normal rats	8 out of 8	32.8 (12–51)

* 1.8×10^8 washed thoracic duct lymphocytes were injected 48 h and 24 h before intravenous challenge with 2×10^5 MC-I cells prepared by trypsinization of tumour. The rats were killed 31 days later.
† Figures in parentheses give range of tumour nodules found.
Group 2 differs from groups 1 and 4 with a significance of $P < 0.001$ and from group 3 with $P < 0.005$. Group 3 does not differ significantly from groups 1 and 4.

Presumably, tumour cells are continuously discharged by the tumour into the blood stream and rapidly settle in the lung. The development of these cells into metastatic growths seems to be prevented in the tumours studied in these experiments by a factor which circulates between lymph and blood. This factor exerts its anti-tumour action in the blood stream or the lung but is relatively ineffective at intramuscular sites. Work is in progress to isolate and purify the active principle from serum. It is unlikely to be a conventional antibody (that is, IgG or IgM) directed against the tumour-specific antigens, because in the serum of rats with these sarcomas no free antibody which combines with the cell membrane of the syngeneic sarcoma cells could be detected by either immunofluorescence or mixed cell agglutination[8]. We are exploring the possibility that the material may be related to the specific macrophage arming factor (SMAF)[9], a substance made by T-cells which combines with macrophages and renders these cytotoxic for tumour cells in an immunologically specific way[10]. Such cytotoxic macrophages have been found in the peritoneal cavity of tumour-bearing mice[11].

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LETTERS TO NATURE

PHYSICAL SCIENCES

Cometary Collisions and Geological Periods

SOME fifteen years ago, I suggested that tektites were produced by collisions of comets with the Earth[1-3]. Many detailed investigations of these objects have added much to our knowledge, and these, together with the lunar investigations, have proved this hypothesis to be very probably correct. I have also suggested that the geological periods were terminated by such collisions, but this was published in the *Saturday Review of Literature*, and no scientist except me, so far as I know, reads that magazine. The energy of such collisions and their frequency was roughly estimated at that time, and the number of these collisions has been reviewed again by Durrani[4].

The energy of cometary collisions has been considered by several authors (see ref. 5), but to estimate this energy more quantitatively, I consider the energy of a Halley's comet type collision. Cometary orbits which extend to great distances have velocities at the Earth's distance from the Sun of 42.1 km s⁻¹; the Earth's velocity is 29.8 km s⁻¹. If the comet collides head on with the trailing surface of the Earth, the relative velocity is 12.3 km s⁻¹; if with the leading surface it is 71.9 km s⁻¹; and if with intermediate positions and directions the relative velocities are intermediate. Of course, the escape velocity of the Earth, 11.2 km s⁻¹, must be added, and is considerable for trailing type collisions. The two velocities, including this correction, are 16.6 and 72.8 km s⁻¹. The higher velocity corresponds to nineteen times the minimum energy. The higher energy collisions are more probable because comets generally cross the orbit of the Earth. The ones in the larger orbits, at least, move markedly toward and away from the Sun, so the Earth sweeps across their orbits. In the present calculations, I use an effective velocity of collision with the Earth of 45 km s⁻¹ though greater or lesser collision velocities are possible.

The masses of comets are largely unknown, but Russell *et al.*[5] and Whipple[6] give reasonable arguments indicating that Halley's comet may have a mass of 2×10^{-9} $M_\oplus$ (~10^{18}) g, and Russell *et al.* suggest that the comet of 1729 may have a mass of 6×10^{21} g. For calculations, I shall use 10^{18} g.

Table 1 gives some estimates based on these assumptions for the effect of a cometary collision with the Earth. The energy, 10^{31} erg, is double the minimum energy required to remove the atmosphere and permit the tektites to be transported to great distances as estimated by Lin[7]. Of course, the energy was not dissipated in only vaporizing water or heating the atmosphere, or heating the ocean and so on, but the data indicate that a very great variation in climatic conditions covering the entire Earth should occur and very violent physical effects should occur over a substantial fraction of the Earth's surface. For example, the great seismic effects might initiate extensive lava flows. The scattering of melted bits of highly siliceous rocks should be only a very small and insignificant part of the physical effects. I suggest that the termination of a geological period would result and a new one would begin.

The scattering of ocean water over land areas would destroy land plants and animals, though probably such water would not fall uniformly and some would not be killed by this method.

Table 1 Energetic Effects a Cometary Collison with Earth Could Produce

Energy to the Earth from Sun in 1 yr	3.48×10^{31} erg
Earthquake of ninth magnitude	2×10^{25} erg
Energy of comet of 10^{18} g and velocity 45 km s⁻¹	10^{31} erg
Fraction of yearly solar energy	0.29
Energy required to remove atmosphere and scatter australites[7]	4.4×10^{30}
If all energy absorbed by	
(1) atmosphere, elevation of temperature	190° C
or (2) ocean water, elevation of temperature	0.175° C
or (3) 100 m of ocean water, elevation of temperature	5° C
or (4) water volatilized at 100° C	4×10^{20} g
Edge of cube to contain this water	74 km
Area of ocean 3 km deep to contain water	1.33×10^{5} km²
or (5) mass which could be thrown in circle about Earth	3.24×10^{19} g
or (6) earthquakes of ninth magnitude	5×10^{5}

The earthquake effect would be great in the immediate neighbourhood of the collision site, and would be noticeable over the entire Earth. The smog effect due to the ammonia and other compounds of the comet would probably be minor. Because the total energy is equivalent to 0.29 of the energy from the Sun for one year, which would raise the temperature of the atmosphere to 190° C if all heat went into the atmosphere, it seems that a considerable rise in temperature would occur. High temperatures for brief periods would be most destructive to animals and plants, and moderate rises in temperature with high humidity would destroy many living things. It seems that sea animals and plants would fare best if located at some distance where shock would not be important. But would this be true of the air-breathing marine dinosaurs? High humidity and air taken into cool bodies would produce considerable condensation of water in their bodies. Of course, other land based reptiles, such as alligators, as well as the primitive mammals and birds, survived from the Cretaceous into the Palaeocene. Such survival could be due to "good luck"—not all areas were equally affected and some animals and plants took the adverse conditions better than others. But it does seem possible and even probable that a comet collision with the Earth destroyed the dinosaurs and initiated the Tertiary division of geologic time.

Were the ages of Tertiary times determined by the fall of comets which produced the tektite fields? Table 2 lists the ages of these recent geologic periods and the ages of tektites. Rough agreement exists. Errors are probably present in both the geological estimates and the physical measurements of the tektite ages which are my averages of recent measurements. Probable errors in the Moldavites, Libyan Desert Glass and the Bediasites are about 2 m.y. The agreement is satisfactory. I wonder if tektites might not be found at some other boundaries between the Eocene, Palaeocene and Cretaceous periods? Lin[7] required nearly as great an energy as calculated here in order to account for the Indochina and Australian tektites, and this produced only a minor discontinuity in geologic strata, so it seems probable that the energy required for the termination of the Cretaceous was much greater than that estimated here.

Table 2 Ages of Geologic Periods and of Tektites

Geologic period	Ages[8] (m.y.)	Ages[9] (m.y.)	Tektites
Pleistocene		0.71 ± 0.10	Australites
	1	1.2 ± 0.2	Ivory Coast
Pliocene			
	13	14.7 ± 0.7	Moldavites
Miocene			
	25	28.6 ± 2	Libyan Desert Glass
Oligocene			
	36	34.7 ± 2	Bediasites
Eocene			
	58	?	?
Palaeocene			
	63	?	?
Cretaceous			

It seems likely that interesting studies could be made by biologists and palaeontologists in regard to the selection of survivors of such catastrophes. It will most probably be millions of years before the next collision occurs, but survivors of such an event would now most probably need to be able to survive the intense radioactivity from nuclear power plants which will be scattered over the entire Earth's surface. As I stated previously, "If the present suggestion gives the true origin" of tektites and also of breaks in the geologic record, "all will agree that any demonstration of the process would cost far more than the scientific knowledge gained would justify."

I am indebted to Professor Shao-Chi Lin for some suggestions in regard to this paper.

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Origin of Elements

WE believe the recent report in *Nature*[1] under this title to be misleading in the light of recent observations. The recent measurement[2] of $a = {}^{12}C/{}^{13}C = 75$ ($+25$, -15) for the ζ Oph cloud is interesting but not surprising because it can be regarded as a confirmation of earlier work[3], as pointed out in ref. 1, and the conclusion that the relative abundance of ${}^{13}C$ in the ζ Oph cloud seems to be terrestrial is quite straightforward. It would be an unwarranted assumption to extrapolate the results from ζ Oph (and other tenuous clouds) to the dense, dusty regions of both the galactic centre and the Orion Nebula.

Zuckerman *et al.*[4] noted the possible presence of regions of high ${}^{13}C$ abundance in both Sgr A and Sgr B2 in their initial detection report of the ${}^{13}C$ isotope for formaldehyde. Whiteoak and Gardner[5] have continued the study of $H_2{}^{13}CO$ and find optical depths which are consistent with a ${}^{12}C/{}^{13}C$ abundance ratio no greater than half the terrestrial ratio—a result which supports an earlier conclusion[6] (from $H_2C{}^{18}O$

observations) that the ${}^{12}C/C{}^{13}$ abundance ratio in Sgr B2 is considerably less than the terrestrial value. In addition, Fomalont and Weliachew[7] have now used interferometric measurements to determine ${}^{12}C/{}^{13}C \sim 25 \pm 5$ for Sgr A and ≥ 20 for Sgr B2. We believe that the abundance anomalies in formaldehyde reported by Zuckerman *et al.*[4] have been substantiated by three independent types of subsequent observations.

Within the solar neighbourhood, the HCN detection report[8] ($J = 1-0$) indicated that the ${}^{12}C/{}^{13}C$ abundance ratio is possibly anomalous in the Orion Nebula; but saturation effects were unknown at the time. Since then, Wilson *et al.*[9] have measured the $J = 2-1$ transition and reported $H{}^{13}C{}^{14}N/H{}^{12}C{}^{15}N$ to be consistent with the terrestrial ratio, a result which has been interpreted to mean that the ${}^{12}C/{}^{13}C$ abundance ratio is probably normal. Subsequently, the hyperfine components of the $J = 1-0$ $H{}^{12}C{}^{14}N$ line were observed in Orion (L. E. S. and D. B., unpublished) and found to have almost normal intensity ratios—suggesting that this line is not heavily saturated and hence $H{}^{13}C{}^{14}N$ may be overabundant. Finally, the recent detection[10] of DCN gives a DCN/HCN abundance ratio more than an order of magnitude greater than terrestrial. Thus abundance ratios determined from measurements of HCN isotopes in the Orion Nebula may well be non-terrestrial; at present the correct interpretation is uncertain.

We note that recent radio measurements[11] of diatomic molecules such as CO give isotopic ratios consistent with terrestrial values in the Orion Nebula. It is possible that simple molecules have abundance ratios close to terrestrial while more complex species do not; thus isotopic abundances may reflect the dominant formation mechanism for each interstellar species. For example, if interstellar CO is formed primarily in the vapour phase, we might expect CO isotopic ratios which are similar to those of the ambient atoms (possibly terrestrial) but, if HCN formation or depletion relies on interstellar dust grains, we may find non-terrestrial HCN isotopic abundances. Optical abundance determinations from diatomic molecules such as CH^+ which are (by necessity) observed in tenuous interstellar clouds should be applied with great caution to dense dusty regions. Finally, although interpretation of radio measurements is often non-trivial, we believe that in the long run radio observations promise to be the most powerful ground-based tool we have for abundance ratios.

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Supersonic Generation of Atmospheric Waves

Chimonas and Hines[1] have pointed out that the Moon's shadow on the Earth's atmosphere during a solar eclipse constitutes a cooling region travelling at supersonic speeds, and may generate atmospheric gravity waves with periods from a couple of minutes up to twelve hours. Atmospheric wave generation by solar eclipses has been observed[2-4], though within the source region (the region of total or partial eclipse) the gravity waves have substantially shorter period than outside it. Here I draw an analogy between the supersonic motion of the Moon's shadow and the supersonic motion of the Earth's terminator. The terminator is supersonic between $\pm 45°$ latitudes at all altitudes below 100 km and may therefore generate gravity waves in this region.

Atmospheric waves are likely to emerge from the regions of solar insolation, namely, the region of molecular oxygen above 90 km altitude, the ozone layer at about 50 km which absorbs solar ultraviolet, the ground, and also possibly from the troposphere where carbon dioxide and water vapour absorb the energy that is reradiated from the ground. It seems unlikely that the tropospheric effect is dominant in the generation of gravity waves because the appropriate high frequency components of the diurnal supersonic motion of the terminator would then be apparent as regular features of ground-based microbarographs. But naturally occurring wavelike fluctuations on ground-based microbarographs are rather rare events that seem to be associated with tropospheric temperature inversions.

The extent of the terminator's source region is far greater than a solar eclipse's source region. At the mesopause the extent of the supersonic motion can be as great as $\pm 55°$ latitude. One would therefore expect atmospheric gravity waves to exist in the ionosphere as a result of the daily supersonic motion of the terminator. This may be the source that is responsible for the almost continuous existence of gravity waves in the ionosphere. If this is indeed the case then a spectral analysis of the gravity waves within the source region should reveal the presence of components of much shorter period than exist outside the source region.

If the trace of the wave's group velocity in the direction parallel to the equator equals the speed of the terminator within the source region an amplification of the atmospheric oscillation should result. If φ is the geographic latitude and θ is the solar declination, which also corresponds to the complement of the angle that the terminator makes with the equator, then to a sufficient approximation in the low and mid-latitudes comprising the source region, amplification of a wave with a horizontal group velocity V_g will occur if

$$V_g = 2\pi R \cos\varphi \cos\theta/(1 \text{ day}) \tag{1}$$

where R is the radius of the Earth. Because $\varphi < 55°$ and $\theta < 23°$ equation (1) shows that $V_g < 0.9$ C where C is the speed of sound. Thus amplification of internal gravity waves cannot occur because, for all internal waves $V_g < 0.9$ C, the only wave types that can satisfy (1) are evanescent oscillations. The characteristic surface wave $\omega^2 = g\,k_x$ which is the fundamental mode of atmospheric oscillation[5,6], can definitely be amplified. Because the group velocity of the characteristic surface wave is $g/2\omega$, substitution into equation (1) shows that at the equator amplification will occur for a period of 8.9 min at the solstices and 9.6 min at the equinoxes. These periods correspond to horizontal wavelengths of approximately 500 km.

So the terminator may generate a strong evanescent oscillation, corresponding to the fundamental mode of the atmospheric oscillation, in the region within which the terminator's motion is supersonic. In this same region there is liable to be a set of internal gravity waves of longer period than the evanescent waves. It is possible that further interval waves may be generated by a resonant interaction with the waves already

extant[7]. Outside the source region a set of internal waves will have been generated in the form of a bow wave. The internal gravity waves outside the region in which the terminator is supersonic will have a longer period than the gravity waves within the source region.

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Magnetic Intensity and Climatic Changes 1925–1970

RELATIONSHIPS between the variations in the Earth's magnetism and climatic changes have been suggested[1-8]. Wollin et al.[7] correlated long-period variations in inclination and intensity

Table 1 Geographical Locations of the Magnetic Observatories selected for this Study and the Percentages of Increase or Decrease of Magnetic Intensity (F) within Period Indicated

Observatory	Latitude	Longitude	% Increase and decrease	Period
Abisko	68° 21' N	18° 49' E	+1	1929–56
Agincourt	43° 47' N	79° 16' W	−5	1900–68
Alibag	18° 38' N	72° 52' E	+6	1904–68
Amberly	43° 09' S	172° 43' E	< −1	1930–64
Apia	13° 48' S	171° 46' W	−1.5	1905–66
Barrow	71° 23' N	156° 44' W	< +1	1949–70
Cheltenham	38° 44' N	76° 50' W	−5	1901–56
Chelyuskin	77° 43' N	104° 17' E	+2	1935–67
Coimbra	40° 13' N	8° 25' W	+1.5	1936–68
College	64° 51' N	147° 43' W	< +1	1941–70
Dickson	73° 32' N	80° 33' W	+1	1933–67
Dombas	62° 04' N	9° 07' E	+3	1916–67
Elisabethville	11° 39' S	27° 28' E	−1	1932–57
Eskdalemuir	55° 19' N	3° 12' W	+1.5	1930–69
Fürstenfeldbruck	48° 09' N	11° 16' E	+2	1939–69
Godhavn	69° 14' N	53° 31' W	< +1	1945–64
Hartland	50° 59' N	4° 29' W	+1.5	1931–69
Helwan	29° 52' N	30° 20' E	+6	1908–59
Honolulu	21° 18' N	158° 06' W	−6	1902–70
Huancayo	12° 02' S	75° 20' W	−5	1922–66
Iasi	47° 11' N	27° 32' E	+4	1931–62
Kakioka	36° 13' N	140° 11' E	< +1	1929–69
Kuyper	6° 02' S	106° 44' E	+1.5	1929–61
Lerwick	60° 08' N	1° 11' W	+2	1933–69
Lovö	59° 20' N	17° 49' E	+2	1929–67
Meanook	54° 37' N	113° 20' W	−2.5	1916–68
Niemegh	52° 04' N	12° 40' E	+2	1931–67
Orcadas	60° 44' S	44° 44' W	−9	1931–62
Rude Skov	55° 50' N	12° 27' E	+2.5	1925–68
San Fernando	36° 27' N	6° 12' W	< +1	1928–68
San Juan	18° 28' N	66° 07' W	−5	1926–70
Sitka	57° 03' N	135° 19' W	−3	1902–70
Sodankyla	67° 22' N	26° 37' E	+2	1930–68
Stonyhurst	53° 50' N	2° 28' W	+1	1925–66
Tenanarive	18° 55' S	47° 33' E	−12	1902–69
Teoloyucan	19° 44' N	99° 10' W	−5	1922–68
Tromsø	69° 39' N	18° 56' E	+2	1933–69
Valentia	51° 56' N	10° 15' W	+1	1936–68
Vassouras	22° 24' S	43° 39' W	−4	1919–68
Voyeykovo	59° 57' N	30° 42' E	+3	1921–68
Witteveen	52° 48' N	6° 40' E	+2	1926–69
Zaymishche	55° 50' N	48° 51' E	+3	1920–64
Zuy	52° 27' N	104° 02' E	+2.5	1928–58

Fig. 1 Annual means of magnetic intensity (*F*) at individual observatories correlated with the 10-yr means of air temperature from nearby weather stations. Opposite trends in intensity and climate can be observed for different parts of the northern hemisphere.
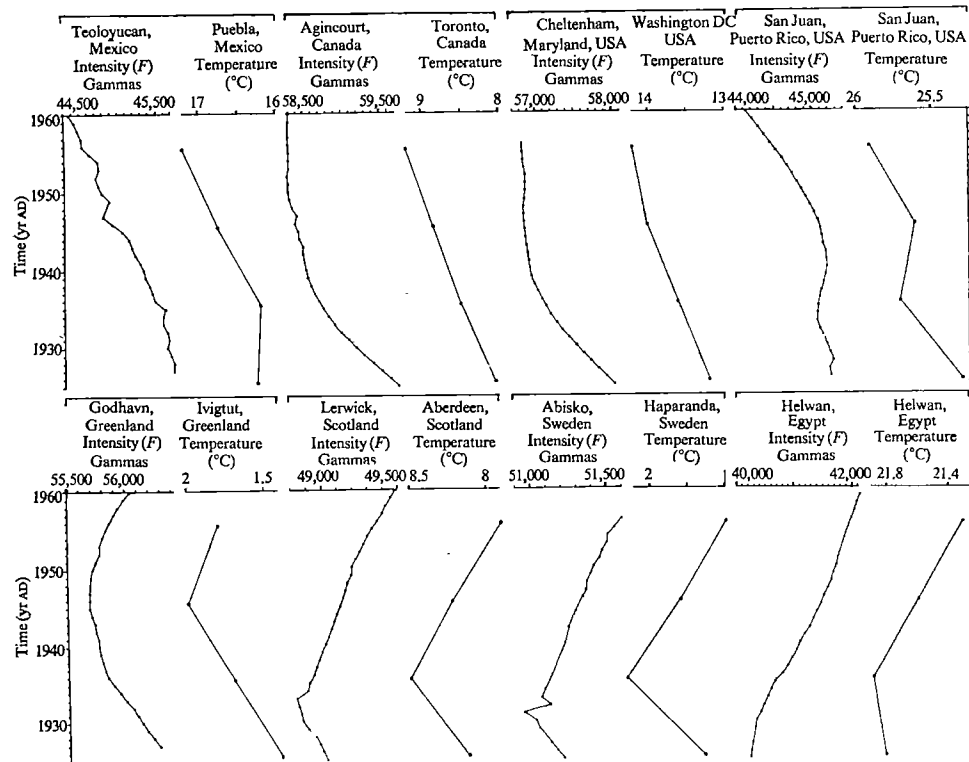
with evidence of climatic changes from deep-sea sediment cores showing a record of about the past 500,000 yr. In addition, they correlated climatic changes with variations in magnetic intensity based on measurements by Bucha *et al.*[9] in archaeological materials from Arizona, Mexico, Europe, and Asia going back to 8,000 yr ago. Wollin, Ericson, and Ryan[8] extended the correlation between long-period variations of the magnetic intensity and evidence of climatic changes from deep-sea sediment cores back to 1.2 m.y.

We report now the results of correlation between short period changes in magnetism and climate, based on direct instrumental observations. The principal objective of this study was to find out if the recent climatic developments could be correlated to some degree with the changes in the magnetic field.

As a source of magnetic data we used the annual means from more than 200 observatories obtained through the courtesy of the Geomagnetic Data Division, Environmental

Data Service, National Oceanic and Atmospheric Administration, US Department of Commerce. As a source of weather data we used the annual and 10-yr means published in World Weather Records[10-13].

We found that the total magnetic intensity (*F*) has been increasing since about 1930 at most of the observatories in the northern hemisphere and decreasing at most observatories of the southern hemisphere and North America. The magnetic observatories selected for this study are listed in Table 1; they all have intensity records at least 30 yr long or shorter records which show abrupt changes. We then compared the intensity records with weather records on local level. Data from magnetic observatories were always compared with records of the nearest weather station.

Fig. 1 shows total intensity curves based on annual means correlated with 10-yr means of air temperature at the nearest weather stations. The intensity is decreasing at observatories in Mexico, Canada, and the United States while the climate is

Fig. 2 Annual means of magnetic intensity (*F*) at individual observatories correlated with 10-yr means of air temperature from nearby weather stations. A comparison of trends in intensity and climate in the northern and southern hemispheres shows that they are opposite for large parts of the two hemispheres.
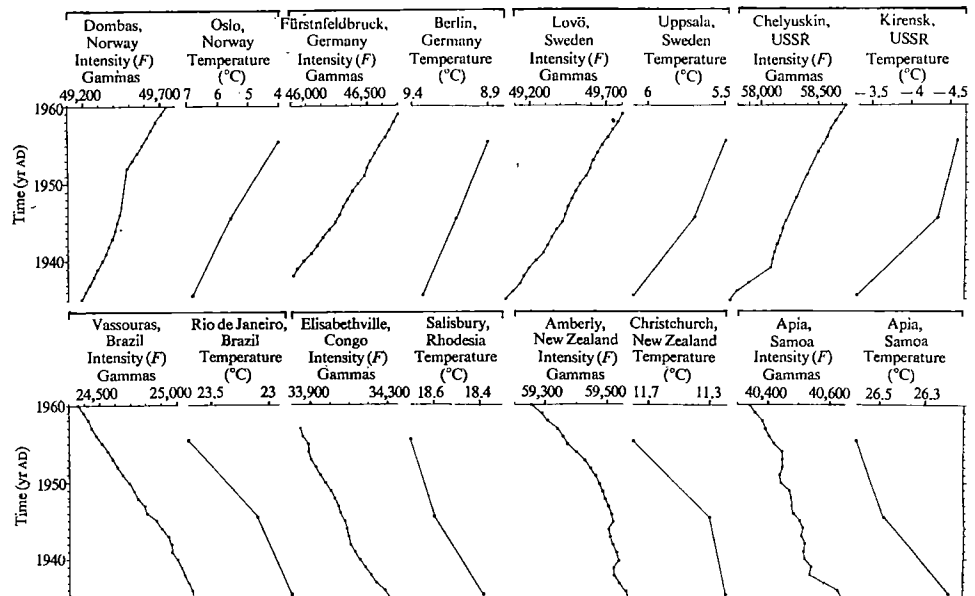
getting warmer. At observatories in Greenland, Scotland, Sweden, and Egypt the intensity is increasing whereas the climate is getting colder.

In Fig. 2 the trends in magnetic intensity and climate at stations in the northern and southern hemispheres are compared. The trends seem to be opposite for large parts of the two hemispheres. The intensity curves from Norway, Germany, Sweden, and the Soviet Union show increase and the climate is cooling. The intensity in Brazil, South Africa, New Zealand, and Samoa decreases and the temperature is rising. As has been pointed out before, a similar relation was found in central and southern parts of North America.

At several stations (a minority of studied cases) the trends of the 10-yr means of air temperature do not correlate with the trends of the magnetic intensity. At some of these stations, however, the intensity trends correlate with the trends of the winter temperature. In Fig. 3 we show an example of such correlation. The intensity curves from Stonyhurst and Eskdalemuir, Scotland, are correlated with 10-yr running averages of winter air temperatures for central England to 1960 (ref. 14) and for 1960 to 1970 (H. H. Lamb, personal communication).

It may be noted that some places where no positive correlation exists between magnetic intensity and air temperature data are under climatic influence of strong oceanic currents. Examples of such places are Sitka, Alaska, Lima in Peru, Gibraltar, and Tokyo in Japan.

At some observatories there are occasionally abrupt changes from year to year in magnetic intensity. These abrupt changes in magnetic intensity are followed by abrupt changes in weather (Figs. 4 and 5). In general, a lag in temperature trends against magnetic variation by at least 1 yr can be observed.
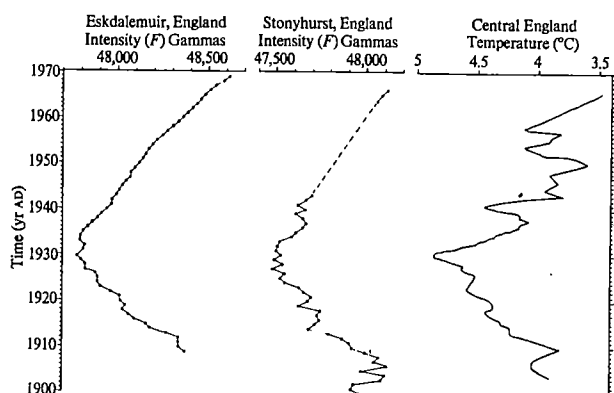
Fig. 3 Magnetic intensity (F) curves based on annual means correlated with 10-yr running averages of winter air temperature for central England to 1960 according to Manley[14] and for 1960 to 1970 according to H. H. Lamb (personal communication).
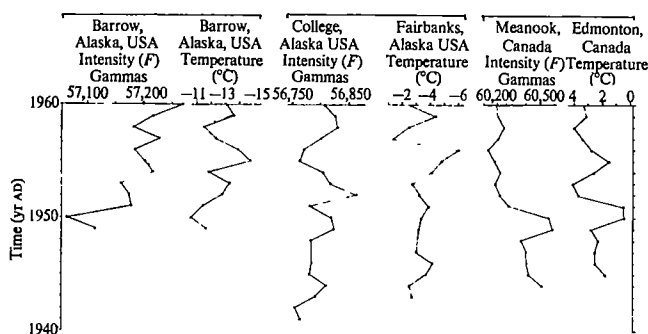
Fig. 4 Correlation of annual means of magnetic intensity (F) from observatories in Alaska and Canada with changes in annual means of air temperature from nearby weather stations. Temperatures lag behind magnetic intensities by one or more years.
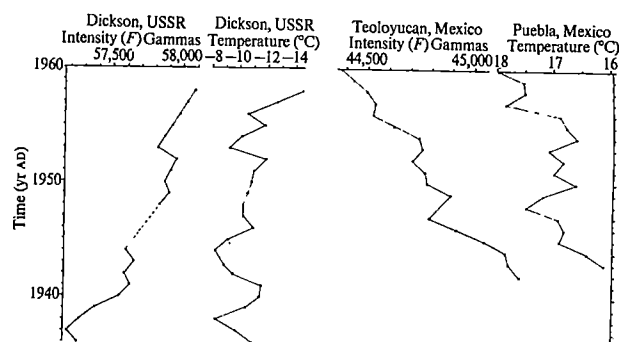
Fig. 5 Correlation of annual means of magnetic intensity (F) from Dickson, USSR, and Teoloyucan, Mexico, with changes in annual means of air temperature trends from nearby weather stations. A 1 yr lag of temperatures behind magnetic intensities can be observed in the Mexican curves.

We have shown correlations between variations in total magnetic intensity and short period climatic changes on a geographical basis. Our tentative conclusion is that the trends in intensity from most of the magnetic observatories in the world with records over at least 30 yr correlate negatively with the 10-yr means of air temperature.

Because of this and other evidence[7,8] we further conclude that a close relationship links changes of the Earth's magnetic field and climate. This may be a direct cause and effect relationship. But Yukutake[15] has suggested that the Earth's magnetic field changes with relation to solar activity and Budyko[16] has shown that the intensity of solar radiation received on ground stations in the northern hemisphere is decreasing since 1938, so we cannot exclude the possibility that both the Earth's magnetic field and climate show parallel reactions to the processes in the Sun.

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Occurrence of Some Chlorinated Aliphatic Hydrocarbons in the Environment

THE total world production of chlorinated aliphatic hydrocarbons probably exceeds 3×10^6 ton yr^{-1} (ref. 1). Some of the compounds concerned are used chiefly as intermediates in the chemical industry (for example, in the manufacture of polyvinyl chloride, aerosol propellants and refrigerants). But others are employed principally as solvents, particularly for degreasing and dry-cleaning. By contrast with the compounds used as intermediates, for which losses to the environment are unlikely to exceed 1–2%, most of those used as solvents will eventually be lost, chiefly by evaporation but also in effluents. Their loss in the United States alone has been estimated to be $\sim 2 \times 10^6$ ton yr^{-1} (ref. 2). Most of the commercially important chlorinated aliphatic hydrocarbons are comparatively stable compounds, and are likely to have reasonably long lifetimes in the atmosphere and aquatic environment. It is likely therefore that the atmosphere and surface waters would contain significant concentrations of them (particularly those used as solvents). At present there seems to be no information available about the levels of these compounds in the natural reservoirs, nor about the extent to which they are concentrated by aquatic organisms. A project has been initiated recently in these laboratories to examine the environmental distribution of the aliphatic chloro-compounds. We present here some preliminary data for air and natural waters.

We describe the methods used for the analysis of air and water samples briefly; a detailed account is to be published elsewhere[3]. For the analysis of air, a known volume (0.01–0.2 m^3) is aspirated through an activated charcoal trap. On returning to the laboratory the chloro-compounds are desorbed by heat-

ing the trap to 250° C in a stream of nitrogen. They are then caught in a cooled trap packed with silicone-coated stationary phase, and are subsequently swept with a current of argon into a gas chromatograph fitted with an electron capture detector. The chlorinated hydrocarbons are stripped from water samples (10–100 ml.) by bubbling with nitrogen[3]. They are then retained in a cooled silicone packed trap and determined by the same technique that was used for gas samples. The estimated coefficient of variation of the method is < 15% for both air and water samples.

Air sampling has been carried out both in rural areas of Britain, away from large towns (central Exmoor and moorlands of North Wales), and over the North East Atlantic along a line between Cap Blanc (Spanish Sahara) and Lands End. In all instances the principal chlorinated hydrocarbons detected were chloroform, carbon tetrachloride, trichloroethylene and tetrachloroethylene. The concentrations of these compounds varied significantly from one station to another (Table 1). No attempt has been made to interpret the distribution pattern because of the small number of samples available. But it seems that, in general, the concentration ranges of these compounds in the air over the sea are quite similar to those over the land away from urban areas. As would be anticipated, air from towns and cities is considerably enriched with these chlorinated hydrocarbons; thus, air sampled in the precinct of this university on March 25, 1972, was found to contain 18 ng m^{-3} of chloroform, 2.3 ng m^{-3} of carbon tetrachloride, 850 ng m^{-3} of trichloroethylene and 68 ng m^{-3} of tetrachloroethylene. The chromatograms from some air samples contained, in addition to the peaks associated with these compounds, other smaller peaks. Peaks arising from dichlorodifluoromethane trichlorofluoromethane and 1,1,1-trichloroethane have been identified. But a number of others have not yet been characterized.

Analyses have been carried out on samples of surface waters collected from the North East Atlantic in August 1972, during a research cruise aboard RRS Discovery to the area south of the Canary Isles. These showed (Table 2) the presence of significant amounts of the same principal chlorinated hydrocarbons that were detected in the air samples. With the exception of tetrachloroethylene, which had a lower abundance, these were present in ratios which were roughly similar to those in air. As with the air samples, there were considerable variations in the concentrations of these compounds from one station to another. Most samples contained traces of dichlorodifluoromethane, estimated at ~ 2 ng l.$^{-1}$. The chromatograms from

Table 1 Concentrations of Chlorinated Aliphatic Hydrocarbons in Air (ng m^{-3})

Sampling location
Land stations

Date	Lat.	Long.	Wind direction	CHCl$_3$	CCl$_4$	CHCl=CCl$_2$	CCl$_2$=CCl$_2$
	51°10′N	04°20′W	200°	4	0.3	28	17
	53°07′N	04°07′W	220°	6	0.4	15	57
	53°03′N	04°02′W	240°	2	0.7	2	8
	58°05′N	03°50′W	220°	—	0.3	4	—.
	53°14′N	03°38′W	220°	2	0.5	4	13
			Average	4	0.4	11	19

Sea stations

Date	Lat.	Long.	Wind direction	CHCl$_3$	CCl$_4$	CHCl=CCl$_2$	CCl$_2$=CCl$_2$
16.7.72	34°19′N	13°32′W	310°	—	0.2	1	3
17.7.72	30°04′N	12°26′W	030°	0.8	0.3	1	8
18.7.72	27°19′N	13°43′W	040°	1.0	0.2	4	2
20.7.72	26°16′N	14°32′W	035°	0.7	0.3	7	2
27.7.72	20°49′N	17°16′W	360°	1.6	0.7	4	7
8.8.72	26°24′N	14°48′W	002°	1.8	0.4	16	3
16.8.72	34°29′N	14°19′W	356°	1.3	0.3	1	1
20.8.72	43°30′N	09°16′W	340°	1.0	0.2	2	5
21.8.72	48°16′N	06°48′W	355°	3.0	0.2	4	1
21.8.72	49°26′N	06°08′W	355°	4.7	0.4	4	9
21.8.72	49°54′N	05°54′W	005°	—	0.6	22	9
			Average	1.7	0.3	6	5

Table 2 Concentrations of some Chlorinated Hydrocarbons in NE Atlantic Surface Water (ng l.$^{-1}$)

Sample No.	Lat.	Long.	Temp. (°C)	Salinity (‰)	CHCl$_3$	CCl$_4$	CHCl=CCl$_2$	CCl$_2$=CCl$_2$
A 37	26°14′N	14°53′W	21.0	36.54	4	0.12	7	0.2
A 46	26°09′N	14°46′W	20.4	36.51	8	0.15	10	0.2
A 47	26°07′N	14°50′W	20.9	36.58	8	0.17	—	0.8
B 12	26°21′N	14°50′W	21.5	36.73	13	0.12	5	0.6
B 13	26°10′N	14°56′W	21.3	36.62	9	0.26	8	0.4
B 14	26°15′N	14°38′W	13.6	26.26	8	0.21	11	0.7
Average					8	0.14	7	0.5

several samples contained other small peaks which it has not yet been possible to identify positively.

The data presented here provide information about the general levels of chlorinated aliphatic hydrocarbons in the atmosphere and the sea. Research is continuing to establish the distribution patterns of these compounds in the ocean and other natural waters. A preliminary investigation has shown that molluscs even from the relatively unpolluted waters around Port Erin, Isle of Man, contain in their tissues significant concentrations of several organic chlorine compounds. These include not only those already detected in sea water, but also a number of others (for example, ∼0.1 p.p.m. of hexachloroethane). Further work is in progress to investigate the involvement of these compounds in the marine biosphere.

We thank Messrs H. M. Dunlop and P. D. Jones for carrying out sampling at sea. Since this work was carried out, Lovelock *et al.*[5] have reported detection of halogenated hydrocarbons in and over the Atlantic.

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Change in the Current Regime in the Suez Canal after Construction of Aswan High Dam

EXCHANGE of water between the Red Sea and the Mediterranean through the Suez Canal takes place in a seasonal pattern. A northward current dominates the Canal from November to June with maximum velocities during winter. This current is reversed in summer to set in a southward direction with maximum velocities in August–September. But the southward current is generally weaker (in velocity and duration) than the winter northward current. This pattern of circulation was established by comparative study of all available monthly observations of salinity from previous years[1].

One of us (S. A. M., ref. 1) observed an unusual distribution of salinity in the Canal on September 29–30, 1966. Comparison with older data from the Canal in September 1924, September 1933, September 1954 and September 1964 showed that the southward current which had hitherto been observed at that

time of the year has been replaced by a weak northward current. Another salinity section was made by El-Sabh on September 17, 1966. The northern part of this section[3], unlike Morcos's section, shows that the northern part of the Canal was filled with Mediterranean water of 38.5–39‰ salinity. This was interpreted[3] as evidence of a southward current. The southern part of the section was published later[4]. Morcos and El-Sabh sections along the southern Canal (between Suez Bay and Great Bitter Lake) show good agreement and indicate a northward flow of the Red Sea water through the Canal.

Strong tidal currents dominate the southern Canal. In winter the northward flood currents are greater in velocity and duration than the southward ebb currents, and as a result the residual non-tidal current is directed northward. In summer opposite conditions occur. The mean sea level at Suez is higher than at the Bitter Lakes in winter, and slightly lower in summer. The currents in the northern Canal depend chiefly on the wind regime and the water balance of the Bitter Lakes, which in turn are a function of the current regime in the southern Canal and evaporation. Evaporation from the Bitter Lakes is an important factor because their surface represents 86% of the total surface of the Canal. In winter part of the water transported northward from the Suez Bay is evaporated in the Lakes and the rest flows to the Mediterranean. In summer, strong evaporation and southward transport to Suez Bay lower the water level in the Lakes, and as a result a feeble current sets northward in the northern Canal aided by the northerly winds and Nile water piling in front of Port Said during the high flood at that time of the year.

The tidal range at Suez is 0.80 and 1.40 m at neap and spring tides respectively compared with only 0.30 m at the northern end of the Canal. The slope of water between the Mediterranean and the Bitter Lakes is much less than between the Lakes and Suez. In the northern Canal, the feeble tidal currents are masked by the non-tidal currents which are much weaker than in the southern Canal, particularly in summer when they become variable in direction with long periods of slack waters (60% of the total time registered by recording current meters in the month of September)[5,6].

The two cruises made in September 1966 show different patterns of salinity distribution in the northern Canal, which may be attributed to the rather slow and variable character of currents in this region. On the other hand, in the southern Canal, where the currents are more stable and dominant, there is a good agreement between the two sections, which confirm the conclusions of ref. 2. Additional support is provided by observations of salinity at Suez during 1966/67 which recently became available[4,7].

Before 1966, the summer southward current in the Canal carried saline water from the Great Bitter Lake to the Suez Bay where higher values of salinity were observed at that season at the southern end of the Canal and even further south in the central part of the Suez Bay. This region is represented in Morcos's observations[1] by station 24 at the most southern buoy of the Canal (162.4 km south of Port Said Lighthouse) and station 25 (164.8 km) at Newport (Zenobia) Lighthouse in

Fig. 1 Seasonal variation of salinity in Suez Bay before and after 1965. *a*, At station 24 (162.4 km, most southern buoy of the Suez Canal). *b*, At station 25 (164.8 km, Newport (Zenobia) Rock Lighthouse). 1954, ref. 1; 1964, our data; 1966, ref. 7; (1966), ref. 4.
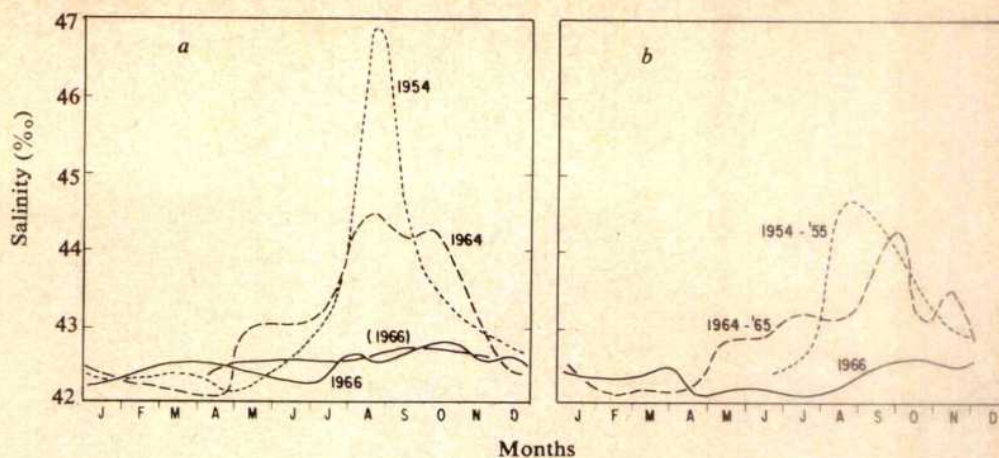
the Suez Bay. We possess monthly observations of salinity for these two stations from the years 1924/25 (ref. 8), 1954/55 (ref. 1) and our observations from 1964/65. Further, monthly observations from 1933/34 exist for station 24 (ref. 9). More recently, salinity at these two stations was observed during 17 hydrographic cruises (most of them fortnightly) by Meshal[7] in the Suez Bay from May 3, 1966, to June 5, 1967, and El-Sabh[4] made five monthly salinity observations at station 24 during 1966. Comparison of salinity before and after 1965 at these two stations (Fig. 1) shows a drastic change in the salinity of the Suez Bay. In 1966/67 the salinity remains without exception below 43‰, and much higher values of salinity are observed from July to October during all the preceding sets of observations in both stations. The maximum salinity observed at 12 m depth at station 24 was 42.81‰ in October 1966, compared with 44.40‰ in August 1924, 44.11‰ in September 1933, 46.94‰ in August 1955 and 44.49‰ in August 1964.

Such a change in the salinity of the Suez Bay confirms that the southward current, which has hitherto occurred in the Canal every summer, did not occur in summer 1966, and that the current remained northward during the whole year. It can no longer be argued that the current was reversed in summer 1966 but was either shorter in duration or occurred earlier than usual because the whole summer of 1966 (July to October) is now represented by seven fortnightly observations[7], all of which show that the salinity of the Suez Bay remained below 43‰, and exclude any possibility of a southward current transporting saline water from the Great Bitter Lake.

In summer 1966, and for the first time, the huge amounts of Nile water which have hitherto flowed in to the Mediterranean were completely prevented by the Aswan High Dam which was finished before the flood of 1966. Whether this change in the current regime is entirely linked to the Aswan High Dam, and whether this change continued to occur every year after the summer of 1966, are questions open to future investigations.

If this phenomenon is permanent biological migration between the Red Sea and the Mediterranean will be promoted. From recent observations of the distribution and ecology of *Ceratium egyptiacum* Halim, Dowidar[10] gave biological evidence confirming the new regime of currents in the Suez Canal.

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Ramgarh Structure, India

CRAWFORD[1], in his letter concerning the Ramgarh structure, a possible impact crater in India, seems not to be aware that the area has now been geologically mapped in detail. During geomorphological mapping of the Lower Chambal Valley in 1968, I encountered this feature and mapped it[2]. My chief findings are that: the Ramgarh dome is, topographically, a circular basin and structurally a dome having quaquaversal dip direction.

This sedimentary dome of typical shape is especially interesting because it displays an inversion of topography. From the Devi temple on the eastern escarpment this basin is seen to be
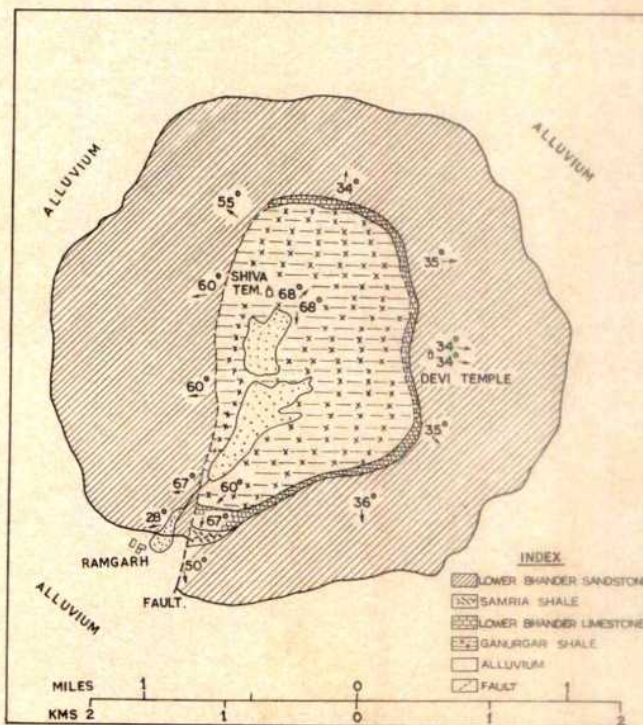
Fig. 1 Geology of Ramgarh dome.

bounded by a precipitating circular wall of Lower Bhander Sandstone nearly 150 m high, underlain by Lower Bhander Limestone and Genurgarh shales which form the lower half of the scarp. The shales are displayed in the form of a circular depression within a dome (Fig. 1).

The amount of dip of Lower Bhander Sandstone ranges from 32° to 70° but mostly close to 35°. Along the western side, the fault contact running north–south brings the Ganurgarh shales and Lower Bhander Limestone in a direct contact with Lower Bhander Sandstones. Because of faulting, the inclination of beds here is unusually high, from 60° to nearly vertical.

The faulting in the dome is indicated by the sudden steep dip of sandstone, truncation of rocks of varying resistance, intense fracturing and close jointing of sandstones and shales, and shattering and brecciation in the sandstones.

Minor folds are also evident in the rocks and are responsible for the local thickening of beds. Within the core of the dome to the east of the Shiva temple, in a streamcut channel, the Ganurgarh shales intercalated with limestone have been exposed. Here the beds plunge towards NNE and SSW at steep angles (about 67°).

Regarding the origin of this dome it seems on the basis of structural and geomorphic features that such a crater-like feature could not have been produced without any support from beneath. Further the Ramgarh dome seems to be a combined result of tectonic and volcanic activity. Thus, the suggestion that this feature is a result of tectonic movement of diapiric nature does not seem convincing.

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Ramgarh Structure, India

CRAWFORD[1] has discussed the possible impact origin of the Ramgarh structure in Rajasthan State, India. He mentioned the find of a shatter coned specimen in the colluvium near the centre of the structure. On the other hand, Auden[2] has commented that the structure may be a kimberlite type of intrusion into the Upper Vindhyans similar to that at Majhgawan in Madhya Pradesh, India. No detailed work has so far been attempted to prove the origin of the structure. The area was visited by Mallet[3] and first mapped on a small scale (1 : 63,360) by Kishen Singh (unpublished). But neither give any conclusive evidence to explain the origin of the anomalous structure.

One of us (A. D.) made an initial visit to the Ramgarh area in July 1972, to find evidence of impact, if any, on the surface in and around the Ramgarh structure. A similar study of the Lonar crater in Buldana district, Maharashtra, India, proved conclusively that that crater is of impact origin (K. Fredriksson et al., in preparation). Samples of rocks were collected from different parts of the Ramgarh structure. Examination of the structure in the field showed abundant evidence of shear fracturing in otherwise massive quartzite. Preliminary microscopic examination of the quartzite has revealed that the quartz grains along closely spaced fractures are granulated and show anomalous birefringence. The evidence, though inconclusive, supports the theory of the formation of the structure by impact.

A detailed investigation of the structure by drilling, pitting and trenching to determine the origin of this controversial structure has been planned by the Geological Survey of India.

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Recent Serpulid Reefs, Connemara, Eire

A SHELTERED lagoon, Ardbear Lough, Clifden, Co. Galway (Irish National Grid L 66 49), provides a very favourable environment for the growth of fringing reefs of the calcareous tubed polychaete Serpula vermicularis L. As far as I am aware living serpulid reefs (as distinct from encrustations) have not been described previously. Fossil reefs are described from the Lower Carboniferous of Cumberland (ref. 1 and M. R. Leeder, in this issue) and sub-fossil reefs from Baffin Bay, Texas[2]. The occurrence of a living serpulid reef is of geological and biological importance and here I describe in outline the ecology of the reefs.

Serpulid reefs occupy about one-third of the area of the lagoon (total area of lagoon about 1 km[2]), chiefly around the perimeter and islands where a rocky substrate is exposed. The lagoon bottom is mud. Shell gravels occur locally in areas of high carbonate production at the lagoon mouth. Terrigenous gravels are found on shores where waves erode glacial deposits.

The biocoenosis is first formed by encrusting and then upward free growth from larvae settling on rock, boulder and gravel sized clasts. Tubes are built so that their apertures face upwards and outwards to a length of up to 20 cm so that the

Fig. 1 Detail of serpulid colony illustrating tubes of Serpula vermicularis (arrows point to trumpet like structures) encrusted with Pomatoceras triqueter, bryozoans and spirorbids.
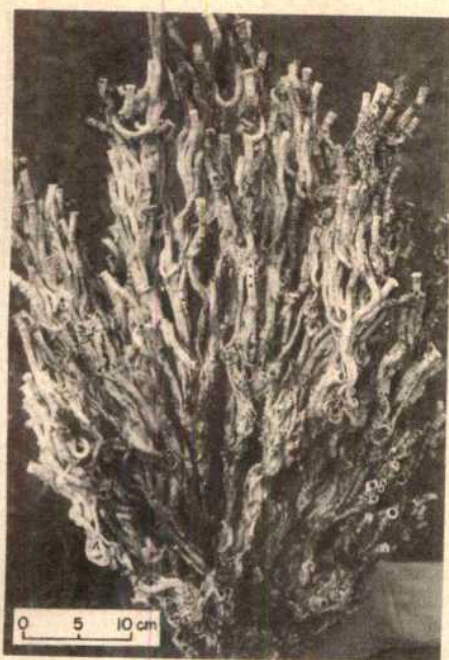
Fig. 2 Section of reef showing growth structures.

worms are positioned most favourably for filter feeding. Increase in colony size follows by larval settlement on old tubes (Fig. 1). Growth of tubes measured over one month (August 1972) averaged 9 mm. Growth is periodic as shown by trumpet-like structures on tubes (Figs. 1 and 2). The older parts of the colony are eroded by algae and sponges, and become very fragile as they age. Segments of the reef frequently break off and lie on the bottom where they form large new areas for larval settlement. This is the principal way in which the reef structure is built upwards and outwards. The greatest reef development occurs at depths between 3 and 19 m where individual colonies may be as much as 2 m high.

The reef provides an attractive site for a varied epifauna which includes the following carbonate secreting organisms: bryozoans, spirorbids, bivalves (byssate sessile) and epifloral calcareous algae. Predators include *Labrus melops* which bites tubes open to feed on the worms and *Asterias rubens* which inverts its stomach down the tube to ingest worms (comparable to the parrot fish and *Ancanthaster planci* of tropical coral reefs).

Currents are not strong enough to transport reef debris or to bring in allochthonous fine sand or larger sized clasts so that an *in situ* carbonate deposit is being formed with a muddy matrix.

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Lower Carboniferous Serpulid Patch Reefs, Bioherms and Biostromes

AUTOCHTHONOUS patch reefs, bioherms and biostromes composed of calcareous-tubed serpulids occur in the Lower Carboniferous (Tournaisian) Lower Border Group of Cumberland and Roxburghshire. Serpulid colonies on this scale were previously unknown in the geological record. Living reefs, from a lagoon in Co. Galway, Eire, have only recently been discovered[1] although dead reefs are common in Baffin Bay, Texas[2,3]. Some of the Carboniferous serpulid horizons were originally discovered by Garwood[4] who briefly referred to them as "worm beds" and assigned the tubes to *Serpula cf. advena* Salter. All the serpulid tubes are calcitic, show concentric microstructure identical to that of recent serpulids, and have small internal diameters (0.5–3.5 mm); an unusual feature is thin septae dividing the tubes (Fig. 3), structures unknown in recent serpulids and which necessitate a complete taxonomic revision.

Thin biostromes and bioherms (Fig. 1b, c) are common in the carbonate members of the Lynebank and Liddel Formations where they may be associated with stromatolites. The tubes within these growth forms are loosely packed and show gently sinuous upward growth. Accretion of the lens-shaped bioherm (Fig. 1b) is thought to have kept pace with quiet water clastic and carbonate mud sedimentation in surrounding areas. The depression at the top of the biostrome (Fig. 1c) is filled with bioclastic debris and indicates a minimum relief of 30 cm during the last stages of growth.

The best developed patch reef is exposed in Stack Cleugh near Bewcastle, where it forms part of the basal limestone of the Main Algal Formation (Fig. 1a). The patch reef, 13 m long and over 2 m high, tongues out to the west into 2 m of thinly bedded calcitic micrites of quiet water origin. To the east the reef reaches a maximum thickness of 2.3 m and ends
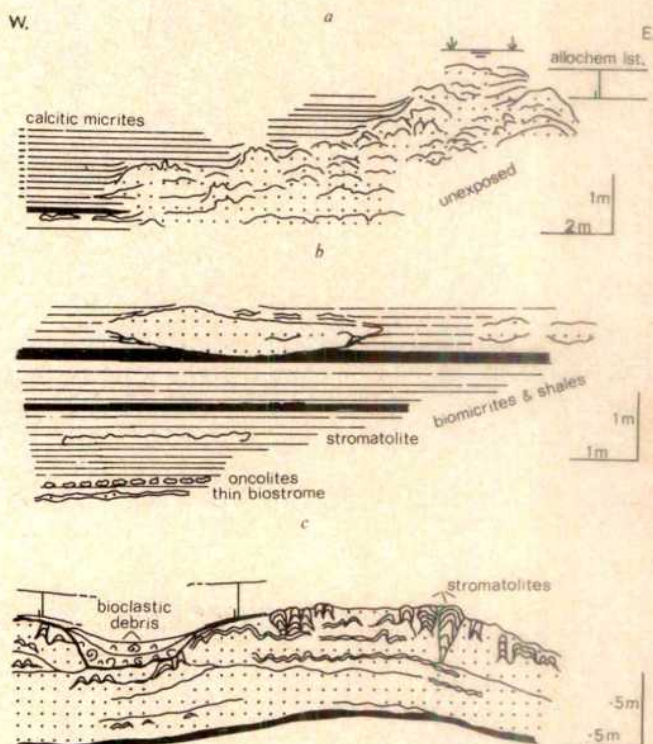
Fig. 1 Field sketches of serpulid colonies. *a*, Patch reef from Stack Cleugh, Bewcastle (NY 58887464), showing internal relief features. *b*, Lens-shaped bioherms from River White Lyne, Bewcastle (NY 54547604), Lynebank Formation. *c*, Part of serpulid biostrome exposed at top of Larriston Quarry, Newcastleton (NY 55739380), Liddel Formation, showing intergrowth of stromatolites in upper part.

Fig. 2 Polished and etched vertical section through ridge growth form from the patch reef shown in Fig. 1a. Thin, closely packed tubes and periodic halts in ridge accretion indicated by dark micritic laminae (arrowed). Scale bar=2 cm.
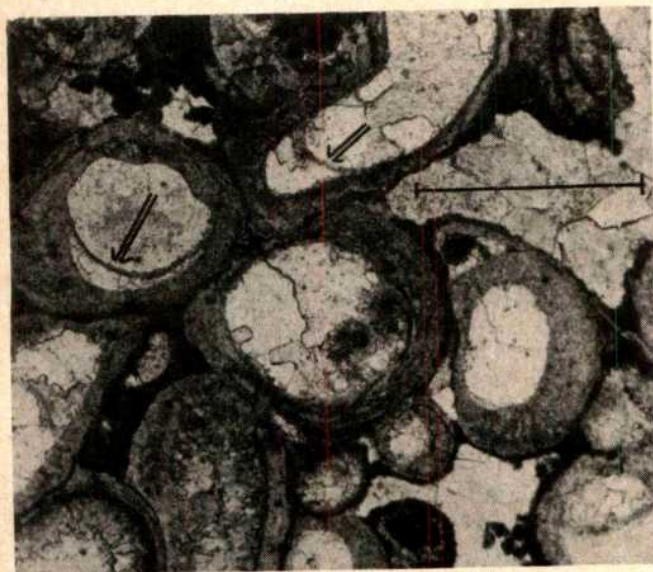
Fig. 3 Photomicrograph to show closely packed, cemented serpulid tubes from ridge growth form of Fig. 2. Septae within oblique sections (arrowed). Tubes infilled with ferroan calcite cement and set in micritic matrix (appears dark) which is partly recrystallized. Scale bar=1 mm.

abruptly along a steeply dipping surface interpreted as original reef topography. Internally the patch reef is composed of mound, ridge (Fig. 2) and dome growth forms up to 30 cm high and 50 cm amplitude. Periodic growth halts are recorded by encrusting micrite laminae of calcareous algal origin (Fig. 2). Individual tubes are tightly packed and serial sections show irregular, sinuous coiling parallel to ridge and dome growth surfaces. Tubes are cemented to adjacent individuals (Fig. 3) and are surrounded by partly recrystallized calcitic micrite matrix containing calcareous algae. Absence of tube debris within the patch reef and in adjacent sediments indicates that the reef formed a compact, resistate structure during life.

Sedimentological work in progress and ecological studies of recent reefs may help explain the significance, dynamics and exceptional development of these fossil serpulid colonies.

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Recent Vertical Crustal Movements between the Dead Sea Rift and the Mediterranean

ANALYSIS of repeated precise surveying of the geodetic network in Israel, presented below, reveals recent crustal movements. The region studied consists mainly of folded sediments disrupted by faulting, which increases in intensity from the Negev in the south towards Galilee in the north (Figs. 1A and 3A). On the east the structure and morphology are determined by the Dead Sea–Jordan Rift (a segment of the East African Rift system) and its subsidiary fractures, tilted blocks and volcanism[1-3]. On the west, a major fault is inferred along the Mediterranean shelf (ref. 4 and Neev and Bakler, personal communication). Much of the tectonic activity is post-Tertiary, but in spite of numerous traces of young crustal activity[5-13], the seismic record indicates a quiet regime with only sporadic stronger tremors[14].

Our study is based on the 1962 and 1969 levellings of the geodetic network in Galilee, and on the 1959 and 1966 levellings of two long traverses across the Negev. The operations conformed to specifications of first-order precise levelling[15,16], the discrepancy (E) between the forward and backward measurement of each segment not exceeding $(3\sqrt{D})$ mm (D, length of a segment in km). Equipment, precision of measurement, and monumentation are of the kind used in study of recent crustal movements in other regions[17-19].

To be significant in a study of recent crustal activity, the differences (dH) between positions of individual benchmarks, determined in two successive surveys, must exceed the range of geodetic errors and must be independent of them. The dH values computed by us range from -65 mm to $+55$ mm (for the 7 yr span) and exceed considerably not only the range of errors based on the adjusted mean square values (0.3–0.6 mm/km), but also the range of errors based on the actual E values (Fig. 2). The plots of both the algebraic and absolute values of dH against those of E, and against D, yield diffuse patterns, a result confirmed also by Kendall rank correlation tests. We assume, therefore, that the dH values obtained in this study are significant and reflect crustal activity. It should be stressed, however, that deep knowledge of all sources of systematic and accidental errors in levelling is still lacking[15].

In regions such as the Russian Platform and Fennoscandia the crust is assumed to rise and sink *en bloc*, and regional rates of movement are often quoted as averages[17-19]. In our case the number of positive and negative dH values is about equal, and averaging them would result in a false picture of apparent stability. However, when the dH are plotted in geological cross-sections and maps, a definite pattern of movement
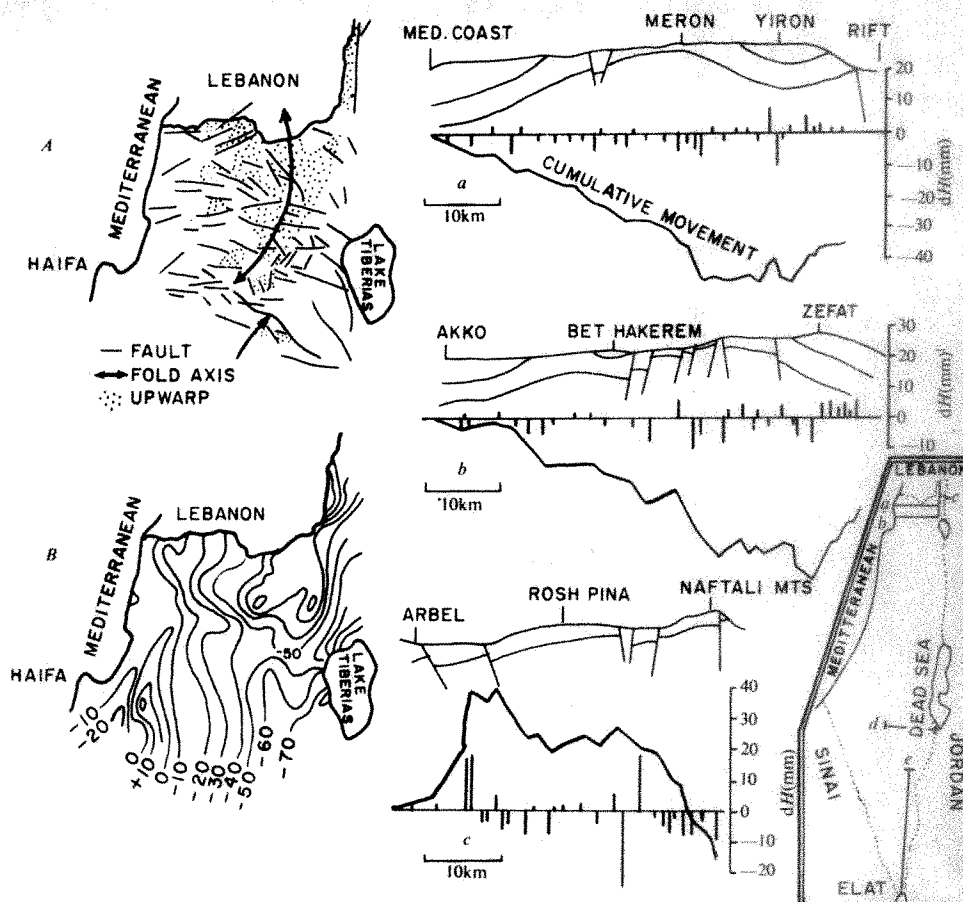
Fig. 1 *A*, Faulting in Galilee; *B*, contour map. *a*, *b* and *c*, Three traverses as shown in inset.

emerges. Fig. 1 shows the distribution of d*H* values in the intensely faulted Galilee. This mountainous region is uparched along a roughly N–S trending axis, but the folding is obscured by three sets of faults, oriented E–W, NE–SW, and NW–SE, which produce complex structures such as tilted blocks in Eastern and Western Galilee, and horsts and grabens in Central Galilee[1-3]. The cross sections indicate a clustering of positive d*H* values along structural lows, and of negative values along the highs. The numerous reversals in sign of d*H* values across faults support the idea that some faults in this region are still active[1]. The relatively sparse spacing of benchmarks does not allow analysis of movement of the individual structures, but the regional pattern is revealed by the contour map of Fig. 1*B*. The contours represent the cumulative d*H*, computed relative to Benchmark F/30 near Akko on the Mediterranean coast; they are therefore contours of displacement relative to an arbitrarily chosen point. The map shows relative sinking of the structural backbone of Galilee with respect to the Rift margins and the coastal zone. It appears also that the d*H* values are somewhat higher along the Jordan Valley segment of the Rift, and along edges of the Yizre'el Valley, where the seismic activity also appears to be higher than in the surrounding areas[14]. No levelling has yet been conducted across the Rift, and the possible movement of its floor cannot be assessed. The N–S cross-section (along the western edge of the Rift), shown in Fig. 1, demonstrates, however, a complex pattern which may be related to the fragmentation of the Rift floor or/and to the subsidiary fractures of the Rift.

Similar relationships were determined in the two traverses across the Negev[20], which is dominated by a series of NE–SW aligned folds locally disrupted by faulting, and transected on the east by the Rift (Fig. 3*A*). Geological evidence suggests young Quaternary subsidence of the Rift interior, accompanied by some differential movements and a rise of the Rift edges[5,7-9,12], some recent faulting, and subsidence of some shallow sabkha zones[12]. The cross-sections in Fig. 3 show the vertical displacements along the levelling paths and confirm

the morphotectonic control of their distribution along faulted as well as folded zones[20].

The above evidence suggests that during the past decade differential vertical crustal movements, up to several centimetres in magnitude, have occurred along the rift borders. The inverse relationship between the morphotectonic features and the d*H* distribution, that is, the subsidence of structural highs and the elevation of lows, is striking and suggests gravity compensation effects. Because, however, the morphotectonic features shown in Figs. 1 and 3 show a close agreement between structure and topography, the question arises whether the d*H* distribution reflects the true displacement pattern or whether it is caused by some unknown operational error related to topography or gravity. Theoretical considerations[21] and step-by-step examinations of the precise levelling techniques and operational procedures have failed to reveal any possible source for such a systematically misleading relationship between the topography and d*H* values.

The magnitude of possible recent crustal activity indicated in this study is similar to that reported from other regions[17-19],
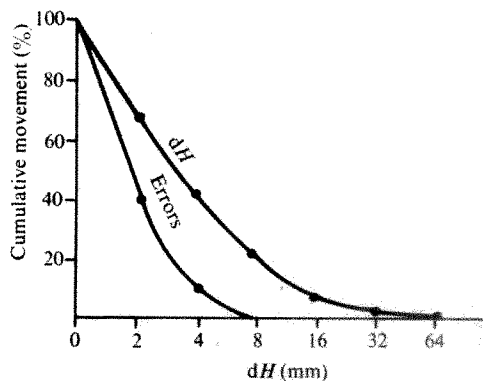
Fig. 2
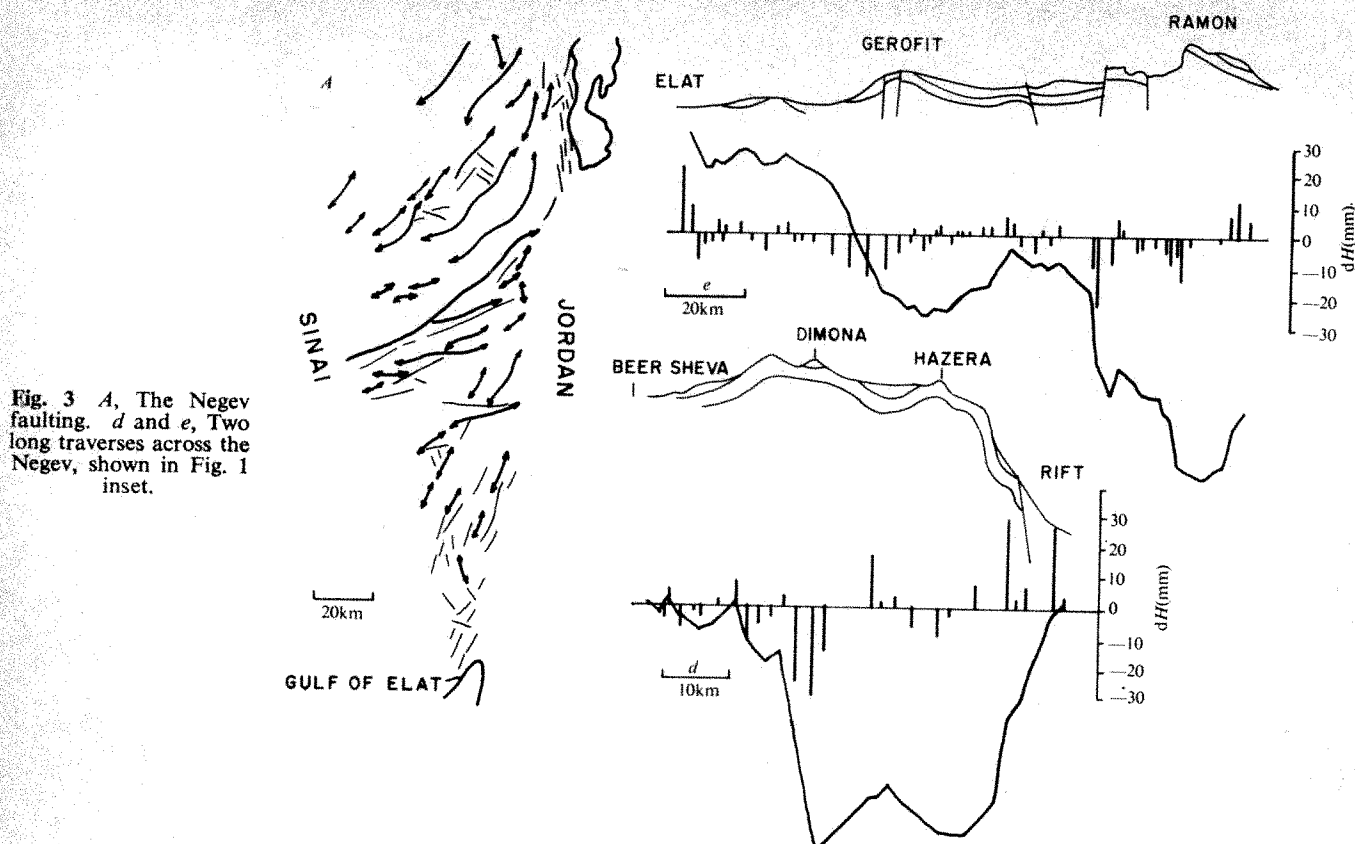
Fig. 3 A, The Negev faulting. d and e, Two long traverses across the Negev, shown in Fig. 1 inset.

but exceeds the long-term rates of tectonic activity, usually quoted in geological literature. Only future levellings will demonstrate whether the movements inferred here persist in signal and magnitude, or whether they oscillate in time and space.

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BIOLOGICAL SCIENCES

Homology between Epstein-Barr Virus DNA and Viral DNA from Burkitt's Lymphoma and Nasopharyngeal Carcinoma determined by DNA-DNA Reassociation Kinetics

THE detection of Epstein-Barr virus (EBV) DNA in established lines of lymphocytes and in biopsies of Burkitt's lymphoma and nasopharyngeal carcinoma has been reported[1-4]. The average number of EBV genomes associated with virus nonproductive cells was estimated as forty to one hundred per cell by a nucleic acid hybridization technique with EBV-specific complementary RNA (cRNA) and cellular DNA[3,4], whereas two to five genomes per cell were found by DNA-DNA hybridization on nitrocellulose filters[1,2].

The number of genome equivalents in Simian Virus 40 (SV40) transformed cells determined by the cRNA hybridization method gave values overestimated ten-fold[5] as compared to DNA-DNA reassociation kinetics studies[6]. The number of EBV genomes in virus nonproductive cells found with the cRNA method was relatively high (0.06-0.2% of the total cell DNA), and might also have been an overestimation due to technique. We therefore conducted DNA-DNA reassociation kinetics studies to re-estimate the number of genomes in nonproductive cells (Raji). This technique also shows whether the virus DNA in test cells or biopsies is identical to the EBV DNA isolated from HR1K (EBV-productive) cells.

Two of the three methods available to produce highly radioactive EBV DNA were unsuitable. It was too difficult to handle the large volume of radioactive culture produced by simple addition of ^{3}H-thymidine and the resultant specific activity was only about 10^4 c.p.m. μg^{-1}; there was no guarantee of uniform transcription of whole EBV DNA by use of reverse transcriptase in vitro with ^{3}H-TTP. The third makes

use of repair-type replication with DNA polymerase I (Kornberg enzyme)[7] and it is reasonable to expect EBV DNA would be evenly repaired at low temperature and therefore evenly labelled with ³H-TTP if nicks are first introduced by small amounts of DNAase I. A low temperature of 15–20° C is required to restrict the reaction to repair-type synthesis without extensive displacement replication of DNA[8]. In this case the reaction initiates with removal of nucleotides from nicked points by activation of 5′ to 3′ exonuclease, and polymerization primed on the 3′ ends of the nicked points follows[7].

EBV DNA was extracted from partially purified virus particles and purified by sucrose gradient centrifugation and two cycles of density equilibrium centrifugation in CsCl as described previously[4].
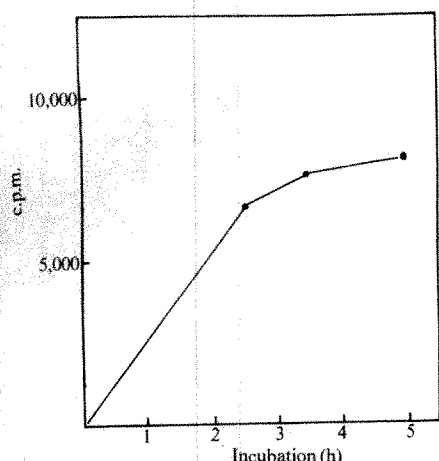
Fig. 1 Time course of ³H-TTP incorporation into EBV DNA by repair synthesis. Two µg of purified EBV DNA was incubated with 0.1 µg of DNAase I at 37° C for 15 min in 1 ml. of the polymerase buffer (potassium phosphate 70 mM, pH 7.4, MgCl₂ 7 mM, and 2-mercaptoethanol 1 mM); the enzyme was inactivated by heating at 70° C for 10 min. This DNA solution was diluted with the reaction mixture so that 1 ml. of the reaction mixture should contain 70 µm of potassium phosphate buffer, pH 7.4, 7.0 µm of MgCl₂, 1 µm of 2-mercaptoethanol, 0.1 µm each of dCTP, dGTP, dATP, 0.3 µm of ³H-TTP (58 c mmol⁻¹), 1 unit of enzyme and 1 µg of EBV DNA. This was incubated at 17° C, and aliquots were taken to measure the incorporation of ³H-TTP into TCA-precipitable materials at 2.5, 3.5 and 5 h.

Fig. 1 shows the kinetics of ³H-TTP incorporation. The reaction approached a plateau in 3 h followed by a slight further increase. It was terminated by addition of 'Sarkosyl 97' to a final concentration of 1% and heating at 70° C for 5 min. Specific activity, determined by measurement of the radioactivity of TCA precipitates of a portion of the reaction mixture at termination (5 h), was 5.25×10^6 c.p.m. μg^{-1} of EBV DNA.

Figs. 2a and 2b show the sedimentation characteristics of template (original) and product (repaired) EBV DNA in native forms, both with a similar distribution with a 10S peak that corresponds to 8×10^5 daltons[10]. Figs. 2c and 2d are sedimentation profiles of the denatured product and template both with a 6 to 7S peak, which corresponds to 10^5 daltons[11], with some trailing toward the higher molecular weight region. There was therefore an average of 6 nicks per native 10S DNA strand. When ¹⁴C labelled DNA from HeLa cells was nicked and repaired with ³H-TTP as described above, the product and the template DNA had the same sedimentation profiles. Incubation with the polymerase therefore did not change the size of DNA.

We estimated the number of EBV genomes in Raji cells, a virus-nonproducing cell, using the highly labelled EBV DNA. DNA was extracted from cells by treatment with pronase, 1 mg ml.⁻¹ and SDS 1% in Tris buffer 0.05 M, pH 9.0, at
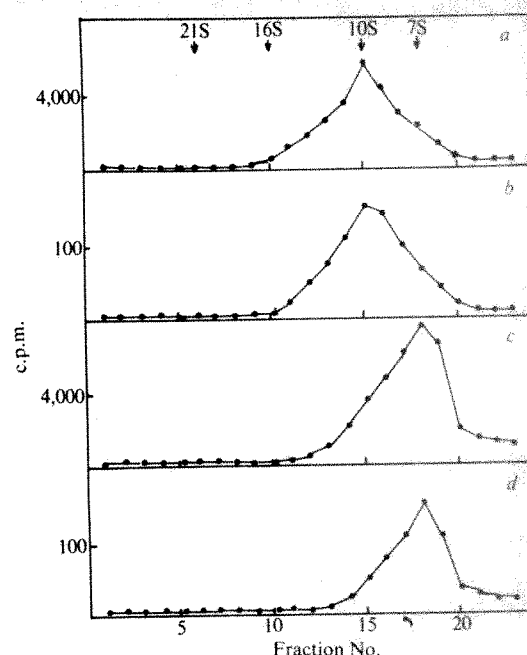
Fig. 2 Sedimentation of EBV DNA product and template in native and denatured form. EBV DNA was originally labelled with ³H-thymidine with a specific activity of 2×10^3 c.p.m. µg⁻¹. This DNA was nicked, reacted with DNA polymerase I in the presence of ³H-TTP (58 Ci mmol⁻¹), and purified. The mixture was passed through 'Sephadex G-25' equilibrated with Tris buffer 0.01 M, EDTA 0.001 M, and 'Sarkosyl 97' 0.1%. The DNA fractions were treated with water-saturated phenol and dialysed against SSC (NaCl 0.15 M, sodium citrate 0.015 M). The most purified fraction (IX) of DNA polymerase I was prepared according to Richardson et al.[9] and had a specific activity of 13,000 units mg⁻¹ of protein determined with dAT polymer as a primer. Centrifugation was conducted at 47,000 r.p.m. for 3 h at 18° C in an 'SW 50.1 rotor' in a gradient of 5 to 20% sucrose, NaCl 1 M, Tris 0.01 M, pH 8.0. ¹⁴C-SV40 component I and II (21 and 16S) DNA were added as markers. The fractions were directly counted on glass filters. a, Native ³H-DNA after the polymerase reaction; b, native ³H-DNA before the polymerase reaction; c, heat-denatured (100° C, 10 min) ³H-DNA after the polymerase reaction; d, heat-denatured (100° C, 10 min) ³H-DNA before the polymerase reaction.

37° C overnight followed by two phenol extractions. The extracted DNA was precipitated with alcohol, dissolved in Tris buffer, 0.01 M, pH 7.2, and EDTA 0.01 M and treated with RNAase, 30 µg ml.⁻¹, free of DNAase for 1 h at 37° C, followed by pronase treatment (1 mg ml.⁻¹, 1 h at 37° C) and phenol extraction twice. The DNA was precipitated, washed with alcohol and dissolved in 0.0025 M EDTA, pH 7.2, and sonicated to reduce the size to $2–4 \times 10^5$ in its native form (determined as in Fig. 2). Cold EBV DNA was also sonicated to the same size. The heat-denatured Raji DNA (500 µg) was mixed with 1.4×10^5 c.p.m. (0.026 µg) of heat denatured ³H-EBV DNA in 1 ml. of phosphate buffer, 0.09 M, pH 6.8 (0.135 M Na⁺). This ratio of cellular DNA to EBV-DNA was equivalent to 2.6 genomes per cell[4] if cellular DNA does not contain any EBV genomes. We used HeLa DNA as a viscosity control; thus 500 µg of heat-denatured HeLa cell DNA was mixed with 1.4×10^5 c.p.m. of heat-denatured ³H-EBV DNA (2.6 genomes/cell) or with 1.4×10^5 c.p.m. of heat-denatured ³H-EBV DNA and 0.06 µg of cold EBV DNA (8.6 genomes/cell). Each glass tube containing 0.1 ml. of the mixture was sealed and incubated at 65° C for each period. The kinetics of reassociation follows the equation $C/C_0 = 1/1 + K C_0 t$[11] where C is the concentration of unreassociated DNA, C_0 is the initial concentration of DNA, t is time, and K is the reassociation constant. At each time indicated in Fig. 3, samples were taken and frozen at −20° C until all the reactions were finished. Single-stranded (unreassociated) and double-stranded (reassociated)
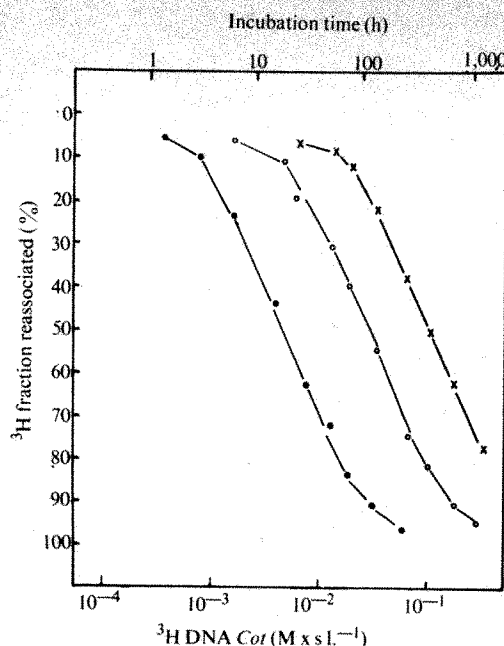
Fig. 3 DNA–DNA reassociation curves for the mixture of Raji DNA and ^{3}H-EBV DNA. 500 μg of sonicated and heat-denatured cellular DNA and heat-denatured EBV–DNA was mixed in 1 ml. of 0.09 M sodium phosphate buffer, pH 6.8, and incubated at 66° C for the indicated period. Single and double-stranded DNA were fractionated through a hydroxyapatite column at 60° C with 0.14 M phosphate buffer containing 0.4% SDS and 0.4 M phosphate buffer containing 0.4% SDS, respectively. ●, 500 μg of Raji DNA and 1.4×10^5 c.p.m. (0.026 μg, 2.6 genomes/cell) of ^{3}H-EBV DNA; ○, 500 μg of HeLa DNA and 1.4×10^5 c.p.m. (2.6 genomes/cell) of ^{3}H-EBV DNA and 0.06 μg (6 genomes/cell) of cold EBV DNA; ×, 500 μg of HeLa DNA and 1.4×10^5 c.p.m. (2.6 genomes/cell) of ^{3}H-EBV DNA.

DNAs were fractionated by hydroxyapatite chromatography (diameter, 1.2 cm ; height, 3 cm) at 60° C[5]. Single-stranded DNA was eluted by 0.14 M phosphate buffer with 0.4% SDS, and double-stranded DNA was eluted by 0.4 M phosphate
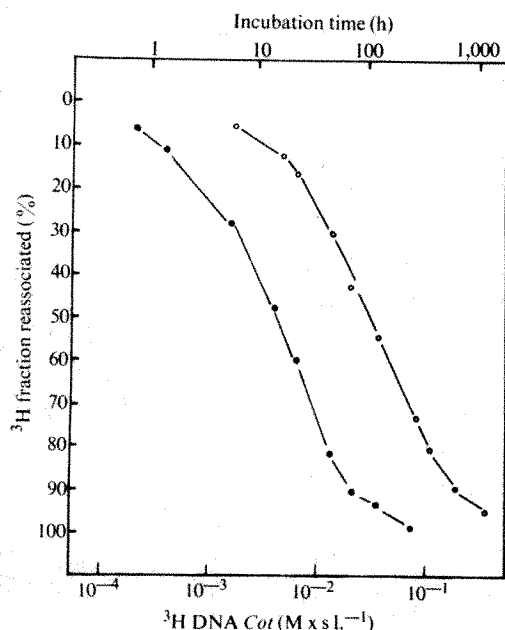
Fig. 4 DNA–DNA reassociation curves for a mixture of DNA from a biopsy of Burkitt's lymphoma and ^{3}H-EBV DNA. ●, 500 μg of biopsy DNA and 1.4×10^5 c.p.m. (0.026 μg, 2.6 genomes/cell) of ^{3}H-EBV DNA; ○, 500 μg of HeLa DNA and 1.4×10^5 c.p.m. of ^{3}H-EBV DNA (2.6 genomes/cell) and 0.06 μg of cold EBV DNA (6 genomes/cell).

buffer with 0.4% SDS. More than 95% of the DNA was eluted in each corresponding fraction when single and double-stranded DNA were chromatographed separately. The effluents were cooled to room temperature and precipitated with cold 5% TCA and counted in a liquid scintillation counter.

Results are shown in Fig. 3. Half C_ot values (50% reassociation) of ^{3}H-EBV DNA with 2.6 genomes/cell and 8.6 genomes/cell were 9.9×10^{-2} and 2.9×10^{-2} M × s l.$^{-1}$ respectively. Thus when the number of genomes was 3.3 times more, the reassociation went 3.4 times faster. The two values agreed well. The half C_ot value of ^{3}H-EBV DNA with Raji DNA was 4.7×10^{-3}. The reassociation occurred 6.2 times faster than with 8.6 genomes/cell and 21.0 times faster than with 2.6 genomes/cell. Thus the total number of EBV genomes present in the mixture of Raji DNA and ^{3}H-EBV DNA was 53.4, calculated from 8.6 genomes/cell and 54.6 genomes from 2.6 genomes/cell. After subtraction of 2.6 genomes of ^{3}H-EBV DNA, the number of EBV genomes present in Raji cells became 50.8 from 8.6 genomes/cell and 52.0 genomes/cell from 2.6 genomes/cell. We have repeated a cRNA hybridization determination for Raji DNA[4] and found 57 genomes/cell, compared with 50 genomes/cell reported by the cRNA method[3]. The number of EBV genomes obtained by association kinetics and by the cRNA method therefore did not show a significant discrepancy.
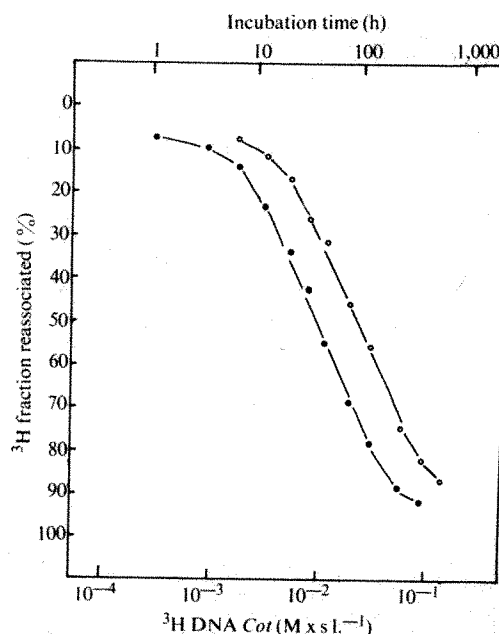
Fig. 5 DNA–DNA reassociation curves for a mixture of DNA from a biopsy of nasopharyngeal carcinoma and ^{3}H-EBV DNA. ●, 500 μg of biopsy DNA and 1.4×10^5 c.p.m. (0.026 μg, 2.6 genomes/cell) of ^{3}H-EBV DNA; ○, 500 μg of HeLa DNA and 1.4×10^5 c.p.m. of ^{3}H-EBV DNA (2.6 genomes/cell) and 0.06 μg of cold EBV DNA (6 genomes/cell).

We have obtained biopsies of Burkitt lymphoma (BL) and nasopharyngeal carcinoma tissue (NPC) (from Professor G. Klein, Stockholm), some of which yielded enough DNA to conduct reassociation kinetics experiments. Procedures were identical to the Raji experiment; the control experiment employing 8.6 genomes/cell was carried out simultaneously. Results are shown in Fig. 4 and Fig. 5. One of the BL biopsies had a half C_ot value of 4.3×10^{-3}; the 8.6 genomes/cell control had a value of 2.6×10^{-2} (Fig. 4). An NPC biopsy showed a half C_ot value of 1.1×10^{-2}; the 8.6 genomes/cell control had a value of 2.8×10^{-2} (Fig. 5). The BL biopsy from these figures contained 49.4 genomes/cell, and the NPC biopsy carried 19.2 genomes/cell ; cRNA

hybridization resulted in 45 genomes/cell and 19 genomes/cell for the same biopsies. Reassociation curves for the DNA of Raji cells, BL biopsy and NPC biopsy showed a pattern identical to control EBV DNA and did not show a biphasic curve which is evidence for partial homology. Thus, Raji, BL biopsy and NPC biopsy contain complete or almost complete viral genomes. We believe this is the first evidence which indicates that the virus DNA in fresh NPC biopsies is not only immunologically related but identical to that in BL biopsies.

Here we have shown that the cRNA hybridization method gives essentially the same number of EBV genomes/cell as DNA–DNA reassociation kinetics. EBV DNA in Raji cells exists as free viral DNA under denaturing conditions[12] in contrast to SV40 DNA in transformed cells[13]. The reconstruction control experiment for cRNA hybridization in which HeLa DNA and EBV DNA are mixed would simulate the condition of EBV DNA in Raji cells[12]. Therefore any preferential overestimation or underestimation of viral DNA should not be expected.

cRNA hybridization is simple and fast for multiple sample analysis, but is not sensitive enough to detect less than two genomes/cell nor does it give the degree of homology. Reassociation kinetics is relatively slow, requiring larger amounts of cellular DNA, but is sensitive enough to detect as little as 0.2 genomes/cell. It is also of use to examine from the shape of the curve whether the viral DNA in biopsies from various sources is partially homologous or identical to EBV DNA, or whether complete or deleted genomes are present. A combination of these two methods and the *in situ* cytohybridization method[14] will be a great help for the study of biopsies related to latent viruses.

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Cell Fusion induced by a Virus within the Zona Pellucida of Mouse Eggs

Mammalian egg cells, like other cells, can be fused in culture in the presence of a virus[1,2]. But because many viruses do not infect eggs which possess a zona pellucida[3], fusion of egg cells has been performed after its removal. This manipulation reduces the rate of successful development in early cleavage eggs[4], which if transferred to recipient oviducts adhere to the epithelium and degenerate[5]. Now we report multinucleation and nuclear fusion within the zona pellucida of mouse eggs injected with a suspension of Sendai virus and somatic cells into the perivitelline cavity.

Sendai virus with a titre of $10^{7.3}$ 50% embryos lethal dose (ELD_{50}) ml.$^{-1}$ was inactivated by ultraviolet light[6] before diluting five-fold with sterile balanced salt solution[7]. Somatic cells from C57BL/6 mice were pipetted into the virus suspension and maintained at 5° C for 15–30 min. For micrurgical manipulation, two- or eight-celled eggs from superovulated BALB/c mice were deposited into a suspension of somatic cells and virus in an "egg-well"[8]. Two to six cervical lymph node[9] or femur bone marrow[1] cells with 5,000–10,000 μm^3 of the suspension were injected into the perivitelline cavity[8] by means of a bevelled micropipette. The micropipette was prepared by grinding at an angle of 35° under a dissecting microscope using a micromanipulator to set the tip on the edge of a water-sprinkled glass wheel, which was surfaced by a No. 600 carborundum and driven by a motor at 850 r.p.m. The pipette orifice, about 10 μm, is good for pipetting somatic cells for viable fusion[10]. It may, however, injure one-celled eggs. Late
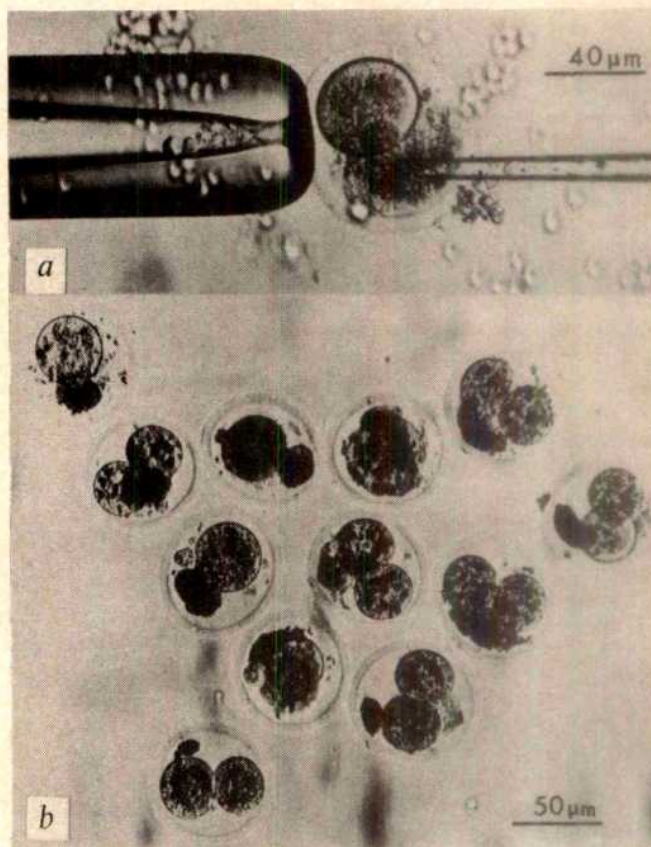
Fig. 1 Micrurgical manipulation of mouse eggs and their development in culture. *a*, A bevelled micropipette entered the two-celled egg and damaged one blastomere. *b*, A group of micrurgically manipulated two-celled eggs was injected with a suspension of Sendai virus and somatic cells and then cultured overnight. The manipulation destroyed one cell. Most of these eggs divided to a two-cell condition; some eggs did not divide (or fused). The unremoved remnant of the destroyed blastomeres in these eggs became a dense mass.
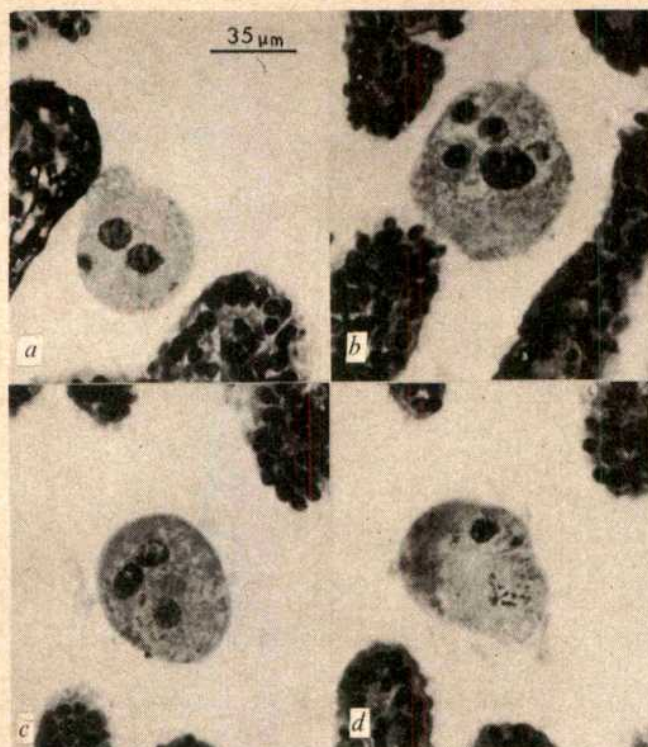
Fig. 2 Cell fusion in developing mouse eggs observed in sections of recipient oviducts. *a*, Originally a two-celled egg in which one blastomere was destroyed and partially removed before a suspension of Sendai virus and bone marrow cells was injected into the perivitelline cavity. The egg divided to restore the two-celled state and then fused in an overnight culture. The zona pellucida of the egg was dissolved in fixation. This section shows two nuclei derived from the fusion of two cells. A remnant of the destroyed blastomere can be seen on top of the fused, multinucleated cell. A somatic nucleus was located at the left edge of the cell. *b*, A section of a morula developed from a virus-injected eight-celled egg. Fusion of a few egg cells in this embryo is evident; the greater mass of nuclear material was apparently derived from the fusion of several nuclei. *c*, Another embryo with a large cell containing two nuclei. *d*, An alternate section of the same embryo showing one nucleus in mitotic metaphase.

two-celled eggs were therefore used after destruction or partial removal of one blastomere (Fig. 1*a*), leaving one viable egg cell[11]. In the eight-celled eggs one or two blastomeres were damaged during injection. Similarly treated eggs which received an injection of balanced salt solution served as controls. The eggs were then cultured at 37° C for two days and observed for division, degeneration, or fusion. Some eggs were incubated 3 h to study early cell fusion; other eggs were cultured 1 or 2 days and transferred to the oviducts[12] of virgin mice for fixation and serial microsectioning.

Table 1 Development of Mouse Eggs in Culture following Micrurgical Manipulation and Injection of Sendai Virus Cell Suspension

Egg stage at start	Egg changes	Eggs developing after an injection containing virus and cells (%) (experimental)*		Eggs developing with injection of balanced salt solution (%) (control)†	
		Day 1	Day 2	Day 1	Day 2
Two-celled (one cell destroyed)	Developing	56	39	57	59
	Degeneration	4	28	0	10
	No change	40	33	43	31
Eight-celled (one or two cells damaged)	Developing	74	52	92	72
	Degeneration	8	21	8	28
	No change	18	27	0	0

* Ninety two-celled eggs and sixty-six eight-celled eggs were injected with virus-cell suspension.
† Fifty-eight two-celled eggs and thirty-six eight-celled eggs were used for the controls.

Two- and eight-celled experimental and control eggs survived in culture (Table 1). After damaging one blastomere of the two-celled eggs, the remaining blastomere divided and restored a "two-celled" stage (Fig. 1*b*) which was equivalent to four-celled eggs if undamaged on the first day of culture. On the second day, many eggs developed to the "four-celled" stage, which normally would have been eight-celled. During culture, some divided two-celled eggs, injected with Sendai virus, fused into a single cell or degenerated more than the control eggs. Fusion of some virus-injected eggs could only be detected by microsectioning.

The eight-celled eggs, injected with the virus-cell suspension or with balanced salt solution (control), similarly developed to early morulae in overnight culture. Some virus-injected eggs developed to late morulae or blastocysts the next day. Blastomere fusion of the virus-injected eggs was also noted.

Serial microsections of nine oviducts were examined. Each received three to four eggs for a total of thirty-four two-celled eggs which had been injected with the virus and somatic cell suspension. Six of these eggs fused as evidenced by the presence of two nuclei (Fig. 2*a*). The presence of a somatic nucleus in an egg was rarely observed. Many somatic cells adhered to the vitelline surface of the eggs after 3 h in culture.

Eight out of eighteen virus-injected eight-celled eggs showed fusion as located in the microsections of five recipient oviducts. Fusion between introduced somatic cells and egg cells inside the zona pellucida was less frequent than fusion between egg cells themselves.

When fusion occurred in "two-celled" eggs within the zona pellucida, it produced a single cell (Fig. 2*a*), whereas in morulae developed from eight celled eggs, only a few cells of the embryos fused (Fig. 2*b* and *c*). During multinucleation, two or more nuclei of egg cells often fused to create a nucleus of greater mass within an enlarged egg cell (Fig. 2*b*). The partial fusion and multinucleation in morulae occurred frequently, producing cytologically unbalanced mosaic preimplantation embryos. Some of the embryonic cells were actively dividing (Fig. 2*d*).

In several preliminary experiments, we have micropipetted a virus-treated lymphocyte or an erythroblast into the perivitelline space to attempt fusion with the vitellus of unfertilized mouse eggs. Sometimes the two cells fused but the somatic cell nucleus did not always reach the middle of the ooplasm. In amphibians, small blastomeres[13] have been used more successfully than embryonic intestinal cells[14] in the nuclear transfer to an unfertilized ovum for development. Our results would indicate that, in the mouse, nuclear cloning of unfertilized eggs with somatic cells by means of virus fusion may not be as easy as with egg cells or small blastomeres.

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Antibody Induced Variation in Malaria Parasites

SUCCESSFUL cellular differentiation and function are dependent upon responsiveness to external stimuli, both useful and harmful, and this responsiveness is particularly evident among some parasitic protozoa. Their environment changes abruptly at transmission from invertebrate vector to mammalian host and becomes potentially harmful when the host mounts an immune response. Several, and possibly most, protozoan parasites avoid total destruction by the immune response they evoke by repeated changes of antigenicity[1]. Replacement of one population by another is detectable in tests carried out at weekly intervals[2,3], and variation at this rate apparently continues for months and perhaps even years. In the absence of suitable techniques for *in vitro* cultivation, the question remained whether this variation resulted from immunoselection or from a form of antigenic modulation. Here I have attempted to clarify this point with one species of malaria parasite, *Plasmodium knowlesi*, using an *in vivo* technique based upon earlier observations[4,5] that *Macaca mulatta*, sensitized with *P. knowlesi* antigen in incomplete Freund's adjuvant, produces high titres of variant-specific schizont-infected cell agglutinating antibodies which were not protective. Animals sensitized in this way were challenged with homologous parasites in numbers small enough to allow detection of possible immunoselection by delay in parasitaemia or failure in the appearance of a new antigenic variant. Results indicated that antigenic variation in *P. knowlesi* is non-selective and that potential for variation on this scale is an integral part of the parasite genome. Three experiments were carried out with similar results, and one is described here.

Two *Macaca mulatta*, approximately 4 kg, were infected with *P. knowlesi* obtained from a frozen stabilate. When the parasitaemias exceeded 30%, schizont-infected cells were harvested for preparation of freeze-thawed *P. knowlesi* antigen, and aliquots of the infected cells were also frozen as a source of stabilate material for challenging sensitized monkeys. Monkeys weighing 2.5 to 4.0 kg were then sensitized with the *P. knowlesi* antigen in incomplete Freund's adjuvant as described previously[4]. After sensitization, they were divided randomly into three groups each of three animals; serum collected at this time from all animals gave a reciprocal schizont-infected cell agglutinin (SICA) titre greater than 10[5]. Three groups of three unsensitized animals served as controls; their sera gave reciprocal SICA titres of less than ten.

An additional monkey was infected with stabilate material isolated at the time of antigen collection, to provide homologous parasites for challenge. At a time when "ring stage" parasites predominated, blood was collected into cold heparinized TC 199 medium containing 5% normal monkey serum, parasitized and total red cells counted, and the blood diluted to the required concentration in the same medium. Groups of sensitized and control monkeys were inoculated intravenously with dilutions equivalent to 10[3], 10[2] or 10 parasitized cells, and their infections monitored by daily blood films. The results are given in Fig. 1.

Schizont-infected cells were isolated for SICA tests, either directly from the challenged monkeys or from normal monkeys
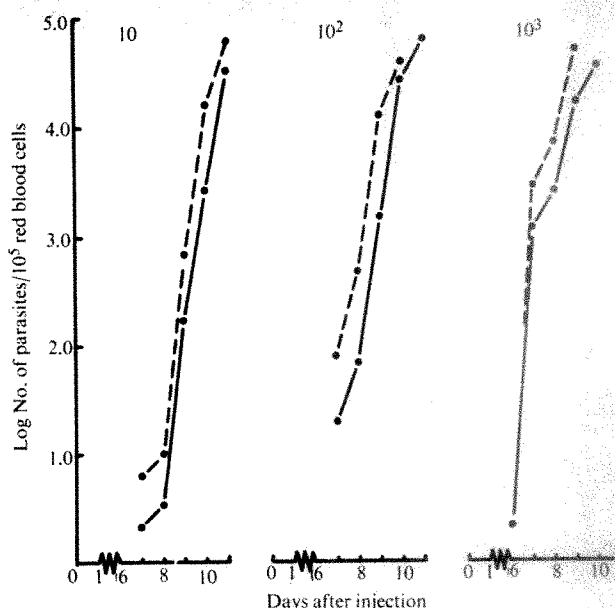
Fig. 1 Geometric mean parasitaemias in groups of *M. mulatta* inoculated with about 10, 10[2] or 10[3] erythrocytes infected with "ring stage" *P. knowlesi*. Three monkeys in each group. ●——●, Sensitized monkeys; ●------●, controls.

receiving an infective inoculum from a challenged animal. The serotypes as determined by SICA tests, using parasites from one monkey in each of the groups receiving 10 or 100 parasites, appear in Table 1; schizont-infected cells were tested against prechallenge sera from both the pre-sensitized or control parasite donors in each group.

Table 1 Schizont-infected Cell Agglutination Tests

Challenge inoculum	Schizont-infected cell donor	Serum donor	Reciprocal log titre
circ. 10	Sensitized	Sensitized	<1.0
		Control	<1.0
		Immune*	5.2
	Control	Sensitized	5.8
		Control	<1.0
		Immune*	<5.8
circ. 100	Sensitized	Sensitized	<1.0
		Control	<1.0
		Immune*	<5.8
	Control	Sensitized	<5.8
		Control	<1.0
		Immune*	<5.8

* Monkey immune after prolonged chronic infection—positive control.

A slight delay of less than 0.5 day in the development of the parasitaemia was detectable in the 3 groups of sensitized animals. This small difference occurred consistently in the three experiments; it was never greater than 0.5 day and was not related to the order in which the monkeys were inoculated. If this delay was due to destruction of parasites in sensitized animals, then comparison of the parasitaemia in sensitized animals receiving 10[2] with controls receiving 10 parasitized cells, and sensitized animals receiving 10[3] parasitized cells with controls receiving 10[2] cells, showed that over half the parasites inoculated into sensitized animals must have survived. Yet this high survival rate was consistently associated in all groups with a complete change of serotype in the sensitized animals and absence of change in the controls (Table 1). Thus the serotype change was apparently not an immunoselective process, but an antibody-induced change in antigen synthesis. The very slight delay in the parasitaemia apparent in the sensitized animals may in fact indicate not destruction of parasites but a

short check in maturation associated with the antigenic change. A more extended delay has been reported in monkeys sensitized with a succession of variants[6].

Variation of the type induced by this *in vivo* technique occurs repeatedly in chronically infected animals and appears analogous to that occurring in free-living ciliates[7]. The stage in the parasite cell cycle at which suitable antibodies can trigger antigenic modification is unknown, as are the molecular mechanisms involved, but analogy with free-living Paramecium suggests that the genome of the malaria parasite carries information for the synthesis of many alternative antigens, presumably with similar function.

Current experiments indicate that the degree of protective immunity shown by a host to malaria infection depends on the relative rate of synthesis of antigen modifying antibodies of the type demonstrated here, and parasiticidal antibodies of equal specificity capable of destroying parasites before they change the appropriate antigens. Increases in the rate of synthesis of parasiticidal antibodies compared with variation-inducing antibodies apparently correlate with greater parasite destruction and thus more protective immunity.

The possibility has been discussed elsewhere[1] that antigenic variation in protozoa might provide a valuable model for other situations where pathogenic cells persist in an apparently immunologically adverse environment. Phenotypic regulation by specific immunoglobulins may also prove to be of importance in non-pathogenic phenomena, as has been suggested in lymphoid cell maturation[8] and avoidance of foetal rejection[9], and possibly represents one way in which phenoclones[10] of cells may arise in development; their action may sometimes involve a degree of sublethal damage[7,11]. Protozoa are useful models for the interaction of environment and genome, both at the molecular and the organelle level[12]. They display in a readily detectable form responsiveness to environmental effects, including specific immunoglobulin binding, less easily observed but none the less important, in other cells at certain crucial stages in their differentiation.

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Transmission of the Chelonian Haemoproteid *Haemoproteus metchnikovi* by a Tabanid Fly *Chrysops callidus*

Haemoproteus metchnikovi (Simond, 1901), also referred to by Garnham[1] as *Simondia metchnikovi*, is a parasite of chelonians. For a number of years we have studied haematophagous insects that feed on turtles in an attempt to discover the mode of transmission of *H. metchnikovi*. Insects were collected, dissected and examined for the presence of intermediate developmental stages and sporozoites. During these studies a sporozoite was found in the salivary glands of the fly *Chrysops callidus*[2] (Diptera: Tabanidae), which gave rise to typical gametocytes of *H. metchnikovi* in erythrocytes when inoculated into laboratory raised turtles, *Chrysemys picta*. We believe this is the first report of a dipteran of the family Tabanidae serving as the intermediate host of a haemosporidian.

Our experimental field site was a pond, located in Oakland County, Michigan, with a natural population of the infected turtle host (*C. picta*) and fly intermediate host (*C. Callidus*). Adult *C. callidus* females were collected as they fed on bait turtles. These flies were dissected, and salivary glands removed and examined microscopically for the presence of sporozoites. Infected glands were placed in a small quantity of 0.75 M saline, broken to release the sporozoites and injected into the peritoneal cavity of laboratory raised *C. picta*. These had been obtained newly hatched and were established and maintained in the laboratory for three and a half to four and a half years, during which time periodic examinations of blood smears were made to ensure they were blood negative for haematozoa. All turtles inoculated with sporozoites became blood positive with gametocytes of *H. metchnikovi*. Our data indicated gametocyte trophozoites were first detectable in erythrocytes approximately 30 to 32 days after inoculation. They grew slowly and mature gametocytes were present in small numbers after approximately three months. We are now studying gametocyte development to maturity within the erythrocyte under laboratory conditions. Because experimental infection of turtles was only recently possible, the sequence of development of the parasite from sporozoite to mature gametocyte in the turtle has not been studied. DeGiusti[3] reported the presence of the megaloschizont in the turtle spleen, but with frozen sporozoite material now available, we are conducting experimental studies which should elucidate the development of the tissue phases within the turtle host.

Table 1 Natural Infection Rate of *C. callidus* with *H. metchnikovi* Sporozoites

	No. flies examined	No. flies infected	% infected
1971:			
June	166	18	11
July	81	23	28
1972:			
June	12	1	8
July	84	32	38
August	44	20	45

The sporozoites of *H. metchnikovi* were present in great numbers (> 1,000) in the salivary glands of *C. callidus*; one or both glands might be infected, and in some heavy infections the sporozoites completely filled the gland lumen. The sporozoites were crescent-like in shape and sometimes recurved on themselves forming short spirals. Motion was limited to sluggish flexing of the body without progressive activity. In smears prepared by drying and methyl alcohol fixation or combined osmic acid-methyl alcohol fixation, the sporozoites appeared as crescent-shaped bodies with one blunt and one tapered end (Fig. 1). In the majority of specimens studied the nucleus is subcentrally located as a single compact mass or split into two or more portions (Fig. 1). Fixed, stained sporozoites measured 9–12 μm in length and approximately 1–1.4 μm in width at their widest dimension.

Oocysts observed in tissue sections of the midgut wall of *C. callidus* were 10–18 μm in diameter. As we do not have experimentally infected flies at present, it is difficult to assess
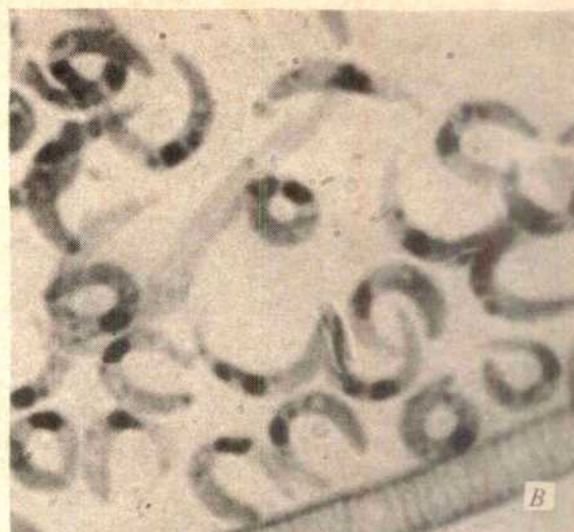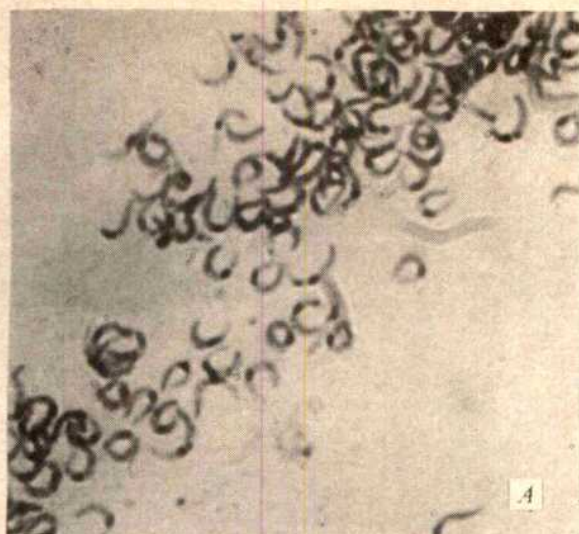
Fig. 1 Crush preparation of *C. callidus* salivary gland showing *H. metchnikovi* sporozoites (*A*, ×1,000; *B*, ×2,560).
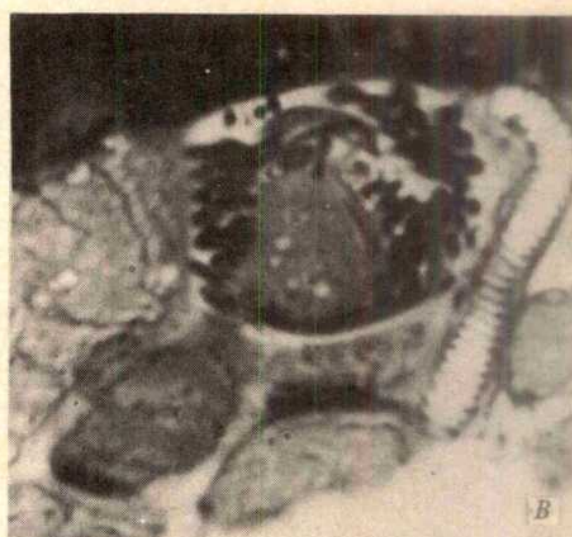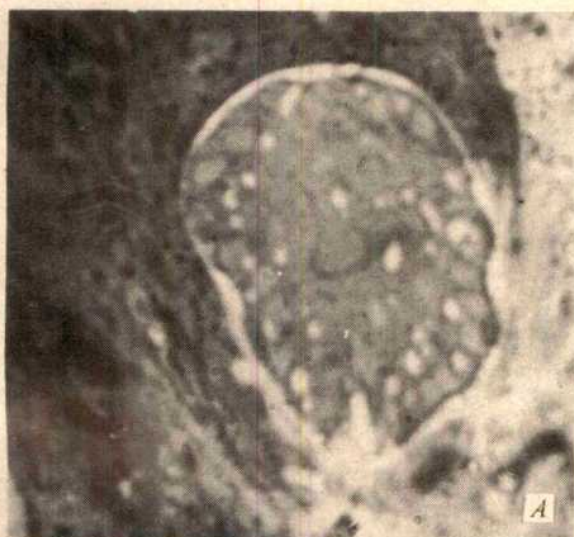
Fig. 2 Oocysts in midgut wall of *C. callidus*. *A*, Young oocyst; *B*, older oocyst with developing sporozoites. ×2,560.

the developmental stages of the oocyst. Those seen range from young stages (Fig. 2*A*) to stages with formed sporozoites (Fig. 2*B*).

Our field studies indicated the season of transmission may be relatively short, as can be seen from the data in Table 1. The earliest fly infections were encountered on June 22, and increased during July and early August, but by mid-August it became difficult to capture or sight flies on turtles, leading us tentatively to conclude that at this time the height of transmission had been reached. Salivary glands examined during this period showed evidence of sporozoite exhaustion; some contained as few as one to five sporozoites, supporting this conclusion. Little is known of the bionomics of *C. callidus*, but the information available indicates that in more southern areas of the US, such as Florida, the flies are active as adults in late April through June[4]. It is quite likely that in a northern area such as Michigan, the adult flies may be active from late May through early September.

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Tracing of RNA from a Puff in the Polytene Chromosomes to the Cytoplasm in *Chironomus tentans* Salivary Gland Cells

THE transport of RNA from the cell nucleus to the cytoplasm is likely to be a composite process, the details of which are far from clear. There is a large discrepancy in molecular size between polysomal mRNA and its tentative precursor, the high molecular-weight, non-ribosomal, nuclear RNA (H RNA)[1]. Also, a considerable part of H RNA does not enter the cytoplasm, but is degraded to acid-soluble products within the nucleus[1]. To explain these findings it has been suggested that H RNA is cleaved to smaller molecules, among which mRNA sequences are selected for transfer to the cytoplasm[2]. In the
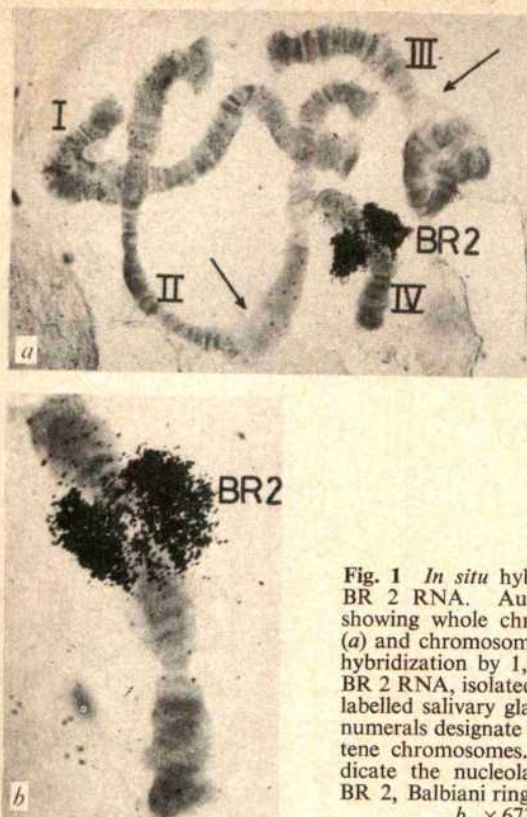
Fig. 1 *In situ* hybridization by BR 2 RNA. Autoradiographs showing whole chromosome set (*a*) and chromosome IV (*b*) after hybridization by 1,000 c.p.m. of BR 2 RNA, isolated from *in vitro* labelled salivary glands. Roman numerals designate the four polytene chromosomes. Arrows indicate the nucleolar organizers. BR 2, Balbiani ring 2. *a*, ×252; *b*, ×672.

study of such transport phenomena it would be advantageous to follow a specific RNA from its site of synthesis in the chromosomes to its functional locality in the cytoplasm. This possibility may be offered in the study of RNA from the giant puff Balbiani ring 2 (BR 2) in the polytene chromosomes of *Chironomus tentans* salivary glands.

Cytogenetic and biochemical studies[3-5] of salivary glands in larvae of Chironomus species have provided a correlation between synthetic activity in the Balbiani rings and the appearance of specific protein fractions in the salivary secretion. It has been suggested that Balbiani rings may produce mRNA for the secretory proteins[4], but this has not been directly demonstrated. BR 2 RNA is present in its corresponding puff as a large molecule with a sedimentation value of approximately 75 S, and appears undegraded in the nuclear sap[6]. Electron micrographs of Balbiani rings reveal characteristic granules of about 400–500 Å in size, which can be traced through the nuclear sap into the pores of the nuclear envelope[7,8]. Although it seems likely, on the basis of these results, that BR RNA does enter the cytoplasm, it has not been possible to show yet. Cytological hybridization may prove to be valuable in this respect, because BR 2 RNA hybridizes specifically *in situ* with its corresponding chromosomal puff[9,10]. Here I have taken advantage of this specificity of BR 2 RNA/DNA hybridization *in situ* to investigate the transfer of BR 2 RNA into the cytoplasm. Labelled RNA was extracted from Balbiani rings, from the nuclear sap surrounding the polytene chromosomes and from the peripheral cytoplasm, and hybridized to denatured squash preparations of salivary gland cells. The location of the ribonuclease-resistant RNA/DNA hybrids was studied by autoradiography.

Balbiani rings and nuclear sap were isolated by micro-dissection of salivary glands which had been subjected to *in vitro* labelling for 90 min with 100 + 100 µCi of tritiated uridine plus cytidine in 50 µl. of modified 'Cannons insect medium'[9]. Cytoplasm was micro-dissected from salivary glands of larvae which had been living for 7 days in ordinary rearing medium supplemented with 1 mCi ml.$^{-1}$ of tritiated uridine and cytidine. Only the peripheral cytoplasm was used, so that in the micro-manipulatory step the nuclei were left intact with a

distinct zone of surrounding cytoplasm in order to avoid nuclear contamination, and only the peripheral zone of cytoplasm was collected.

The labelled RNA was liberated by dissolution of the micro-dissected samples in droplets of Tris buffer (*p*H 7.4) containing pronase (1 mg ml.$^{-1}$) and sodium dodecyl sulphate (5 mg ml.$^{-1}$). The droplets were incubated for 3 h in 37° C, and then diluted with 75 µl. of 2×SSC. This solution was heated for 5 min at 100° C to reduce the molecular size of the RNA[9]. Squashes of salivary gland cells were made and treated with ribonuclease. Denaturation of DNA *in situ* was accomplished by treatment of the slides in 90% formamide in 0.1×SSC at 63° C for 2.5 h. Ten µl. of the labelled RNA in 2×SSC was added to each squash preparation, which was then covered by a cover-slip and incubated for 4 h at 63° C in sealed Petri dishes. The hybridization was interrupted by immersing the slides in ice-cold 2×SSC. The slides were subsequently treated with ribonuclease (100 µg ml.$^{-1}$ of 2×SSC, 2 h at 37° C), and extensively washed in 2×SSC. Autoradiographs were prepared with 'Kodak AR 10' stripping film, and the slides were exposed for 2 months.

Preparations challenged with BR 2 RNA showed distinct labelling in the BR 2 region of chromosome IV, and comparatively few grains were seen outside this region (Fig. 1*a* and *b*). The nucleolar organizers were not labelled (Fig. 1*a*). Neither RNA from chromosomes I, II or III, nor nucleolar RNA, gave rise to a significant number of grains in the BR 2 region[9]. Consequently, *in situ* hybridization with BR 2 RNA is specific in labelling only its corresponding puff region. The heavy labelling over BR 2 in these preparations indicates that BR 2 contains repeated DNA sequences. A similar conclusion was drawn from analyses of quantitative and kinetic hybridizations between BR 2 RNA and filterbound *Chironomus tentans* DNA[10].

Nuclear sap RNA hybridized in a fashion similar to that of BR 2 RNA, the difference being mainly a slightly higher number of grains over the chromosomes (Fig. 2*a*). The BR 2 region of chromosome IV was heavily labelled (Fig. 2*b*) which indicates the presence of BR 2 RNA in the nuclear sap. This result agrees with previous experiments[11,12] in which the proportion of BR 2 RNA out of total, newly synthesized, nuclear sap H RNA was estimated to be at least 50%.
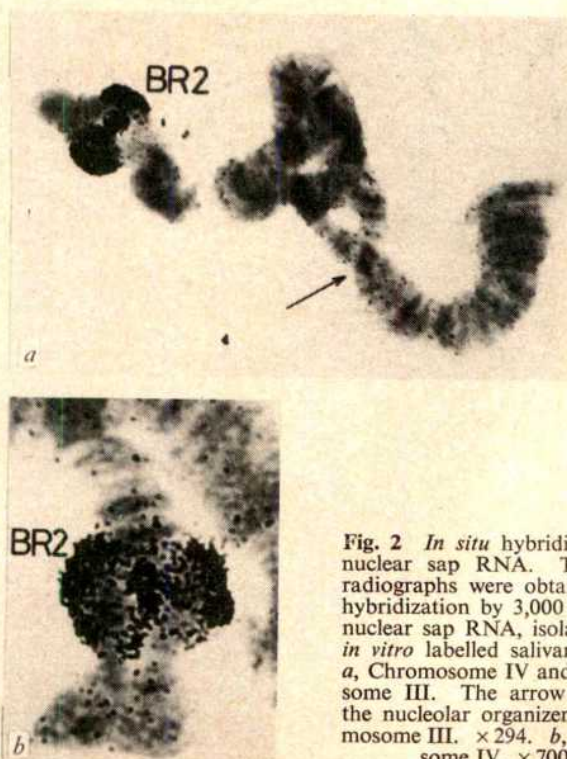
Fig. 2 *In situ* hybridization by nuclear sap RNA. The autoradiographs were obtained after hybridization by 3,000 c.p.m. of nuclear sap RNA, isolated from *in vitro* labelled salivary glands. *a*, Chromosome IV and chromosome III. The arrow indicates the nucleolar organizer of chromosome III. ×294. *b*, Chromosome IV. ×700.

In the preparations hybridized with cytoplasmic RNA, most of the grains were again found in the BR 2 region of chromosome IV (Fig. 3), but a weak labelling was frequently observed also in the nucleolar organizers (Fig. 3a). An additional large puff on chromosome IV, Balbiani ring 1, was labelled, although with fewer grains than BR 2 (Fig. 3b). The finding of grains over the nucleolar organizers after hybridization with cytoplasmic RNA (Fig. 3a) but not after hybridization with nuclear sap RNA (Fig. 2a) was expected. Labelled ribosomal RNA accumulates in the cytoplasm during a long-time in vivo labelling[13], but enters the nuclear sap only to a very small extent during the 90 min in vitro labelling[13].

The number of grains in the BR 2 region after hybridization with cytoplasmic RNA (Fig. 3b) is significant, but smaller than after hybridization with in vitro labelled BR 2 RNA or nuclear sap RNA. This may be explained by the smaller isotope concentration used in the in vivo labelling of larvae, which will result in RNA with a lower specific activity. In addition to this, cytoplasmic dilution by pre-existing unlabelled BR 2 RNA might have taken place. Nevertheless the significant labelling in the BR 2 region obtained after hybridization with cytoplasmic RNA clearly shows that BR 2 RNA is present in the cytoplasm. In control experiments run in parallel to those shown in Fig. 3, it was found that RNA, extracted from the nuclei of those in vivo labelled glands which had been used for cytoplasmic extraction, failed to give a significant number of grains over the chromosomes and Balbiani rings. This probably means that the amount of intranuclear, in vivo labelled BR 2 RNA is too small to be detected by the technique. Consequently, the positive results by using the cytoplasmic RNA suggest that an accumulation of BR 2 RNA takes place in the cytoplasm during the 7 days in vivo labelling.

The significant labelling in the BR 1 region (Fig. 3b) after hybridization with cytoplasmic RNA indicates that RNA from this puff is also present in the cytoplasm. In a previous study[10] it was shown that BR 1 RNA is able to hybridize with its corresponding puff in a way very reminiscent of BR 2 RNA hybridization, although the number of grains over BR 1 was always smaller. On the basis of those results it was suggested that BR 1 also contains repetitive DNA[10]. Label in the BR 1 region has also been observed after hybridization with nuclear sap RNA, although this is an infrequent finding. This variability could be related to biological differences between animals, because BR 1 is not always apparent, and it seldom reaches the size of BR 2. In the present experiments nuclear sap and cytoplasmic RNA came from different animals.

My demonstration of Balbiani ring RNA in the cytoplasm extends the previous line of ultrastructural[7,8] and biochemical[6,9,11] evidence, suggesting a peripheral transport and possible involvement of BR RNA in translational processes. The presence of BR RNA in the polysomes, however, remains to be shown, as well as its further processing in the cytoplasm.

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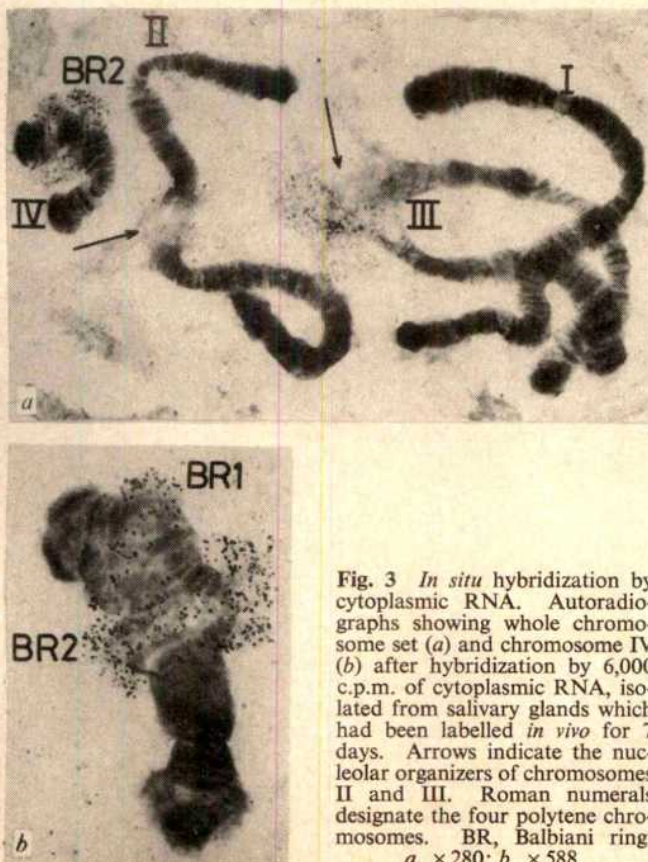
Fig. 3 In situ hybridization by cytoplasmic RNA. Autoradiographs showing whole chromosome set (a) and chromosome IV (b) after hybridization by 6,000 c.p.m. of cytoplasmic RNA, isolated from salivary glands which had been labelled in vivo for 7 days. Arrows indicate the nucleolar organizers of chromosomes II and III. Roman numerals designate the four polytene chromosomes. BR, Balbiani ring. a, ×280; b, ×588.

Conversion of the Sex Pheromone of the Cabbage Looper

THE mechanisms by which airborne molecules stimulate the olfactory receptors of insects remain largely undefined. In the Insecta, antennal sensilla contain pores which connect the external environment with the receptor membrane of the dendritic nerve endings[1-3]. The ultimate fate of the stimulant molecule that enters the pore is not yet known. Unpublished data cited by Schneider[1] and Kaissling[4] indicated that bombykol (E)-10, (Z)-12-hexadecadien-1-ol, was progressively metabolized into acid and ester after absorption on the antennae, or other body parts of males and females of Bombyx mori (L.). This finding cannot be directly correlated with any specific step in the olfactory mechanism, but it suggested that an enzymatic process might be involved at some point. Other indications of chemical stimulants interacting with protein substances in the antennae of insects have been reported[5,6].

We report a protein binding process and an enzymatic process in antennal homogenates of the cabbage looper, Trichoplusia ni (Hübner), which may be involved in the perception of pheromone. The cabbage looper was chosen for several cogent reasons: (a) the behavioural responses to the sex attractant ((Z)-7-dodecen-1-ol acetate) and various related chemicals have been well studied[7,8]; (b) electrophysiological studies have been completed with all the chemicals used here (to be reported); and (c) all chemicals and pheromones were available in high purity (95% + purity; the synthetic pheromone sample contained no measurable (Z)-7-dodecen-1-ol by GLC analysis).
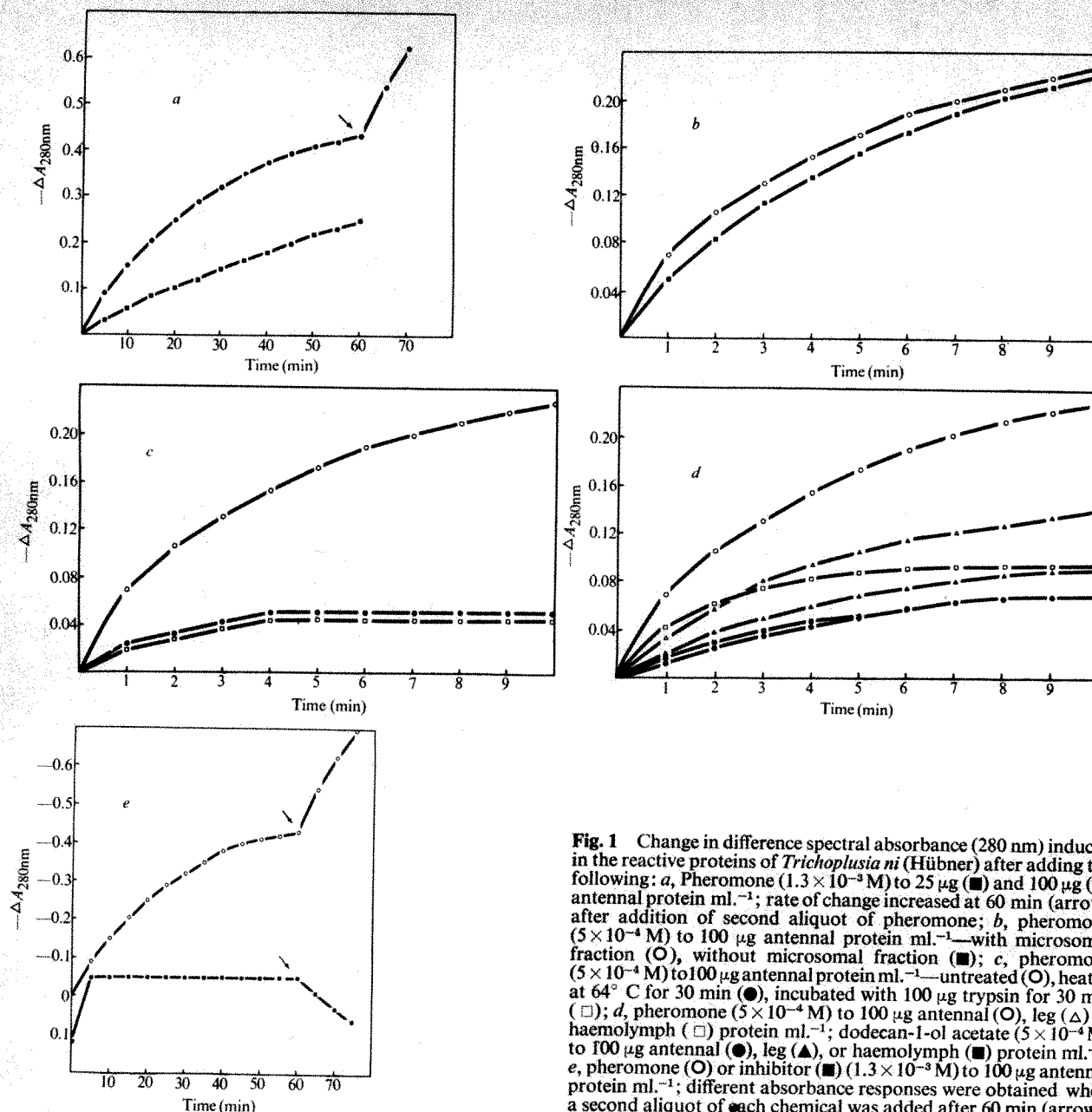
Fig. 1 Change in difference spectral absorbance (280 nm) induced in the reactive proteins of *Trichoplusia ni* (Hübner) after adding the following: *a*, Pheromone (1.3×10^{-3} M) to 25 µg (■) and 100 µg (●) antennal protein ml.$^{-1}$; rate of change increased at 60 min (arrow) after addition of second aliquot of pheromone; *b*, pheromone (5×10^{-4} M) to 100 µg antennal protein ml.$^{-1}$—with microsomal fraction (O), without microsomal fraction (■); *c*, pheromone (5×10^{-4} M) to 100 µg antennal protein ml.$^{-1}$—untreated (O), heated at 64° C for 30 min (●), incubated with 100 µg trypsin for 30 min (□); *d*, pheromone (5×10^{-4} M) to 100 µg antennal (O), leg (△) or haemolymph (□) protein ml.$^{-1}$; dodecan-1-ol acetate (5×10^{-4} M) to 100 µg antennal (●), leg (▲), or haemolymph (■) protein ml.$^{-1}$; *e*, pheromone (O) or inhibitor (■) (1.3×10^{-3} M) to 100 µg antennal protein ml.$^{-1}$; different absorbance responses were obtained when a second aliquot of each chemical was added after 60 min (arrow).

Antennae from male moths (400 pairs, approximately 25 mg wet weight) were homogenized in 4.0 ml. of 0.5 M sucrose buffered with 0.05 M Tris-HCl, *p*H 7.5 at 4° C. The homogenate was centrifuged at 20,000*g* for 45 min and the supernatant was decanted. The protein content was determined by the method of Lowry *et al.*[9].

Binding of the sex attractant and its analogues to soluble antennal protein(s) was measured by ultraviolet difference spectroscopy[6,10,11]. Difference spectra recorded from 220 to 350 nm on a dual-beam recording ultraviolet-visible spectro-photometer, obtained with the antennal supernatant, the pheromone, and the pheromone analogues, indicated a time-dependent maximal negative peak at 280 nm. Subsequent measurements of the negative absorbance difference ($-\Delta A$ or negative change in optical density units) relative to the baseline at 280 nm were recorded with a single-beam ultraviolet-visible spectrophotometer. Baselines (zero absorbance (optical density) as a function of 280 nm) were attained by electronically neutralizing the original absorbance of the antennal preparation and the chemical stimulants with the absorbance control system (total absorbance negated was less than 1.0 OD unit). Full scale sensitivity of the recording system was set at 0–0.5 A, and the temperature of the cell compartment was thermostated at 20° C.

Twenty-five µl. of a sonicated solution of the pheromone in distilled water (final concentration 1.3×10^{-3} M) was added to 25 µg of antennal protein in 1 ml. of 0.05 M Tris-HCl, *p*H 7.5. The rate of absorbance change ($-\Delta A$) at 280 nm was dependent on the concentration of the antennal protein (Fig. 1*a*). As the concentration of protein was increased, the rate of change in absorbance also increased. After 1 h, the rate of absorbance change had diminished, but was reactivated by addition of another 25 µl. of pheromone.

A 2 ml. aliquot of the antennal supernatant was centrifuged at 105,000*g* for 2 h to remove the microsomes. The resulting particle-free supernatant reacted with the pheromone (5×10^{-4} M) with only a slight loss in activity (Fig. 1*b*). The activity of the antennal supernatant, however, was destroyed by heat at 64° C or incubation with 100 µg of trypsin (*p*H 7.5) at 20° C for 20 min (Fig. 1*c*). These results demonstrated that the monitored absorbance change involved interaction of the pheromone with soluble protein in the antennae. This suggests the interaction was enzymatic because the gradual change in absorbance was more characteristic of an enzymatic reaction than of nonenzymatic binding[10]. If the absorbance change had been due only to pheromone binding or complexing with antennal protein, then the change in absorbance should have rapidly reached a plateau that would have been dependent on the

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concentration of the two reactants, antennal protein and pheromone.

To determine whether the reaction was unique to the antennae, particle-free supernatant fractions of haemolymph and legs were prepared and assayed for pheronome reactivity (Fig. 1d). The leg proteins were less active than the antennal proteins, and the haemolymph proteins were even less active. No measurable reaction occurred when pheromone was incubated with bovine serum albumin. However, preparations from the antennae of females were as reactive as the male preparations. A behaviourally inactive saturated analogue of the pheromone, dodecan-1-ol acetate, was assayed with the antennal, leg and haemolymph protein preparations. There was less reaction with dodecan-1-ol acetate in all three preparations than with the pheromone. These results indicate that the reactive protein showed some specificity for the pheromone and was primarily localized in the antennae.

To demonstrate more conclusively that interaction of the pheromone with the antennal supernatant was enzymatic, we monitored the rate of pheromone disappearance during the incubation with antennal proteins by gas chromatography[12]. Sonicated pheromone in distilled water (final concentration 2.02×10^{-2} M) was incubated with 2.0 ml. of antennal homogenate (100 mg wet weight ml.$^{-1}$), 0.2 ml. aliquots were collected during the reaction at 20° C and each aliquot was extracted with 0.5 ml. of anhydrous ether. One 0.2 ml. sample was held in a boiling water bath for 15 min before a 60 min incubation and then extracted. Gas chromatography of this sample gave one peak with a retention time identical to that of the pheromone. All other samples gave two peaks, one that represented the pheromone and a second one that had a retention time identical to that of (Z)-7-dodecen-1-ol, the alcohol moiety of the pheromone, which is a potent inhibitor of male attraction to the pheromone[12]. A time-dependent reduction in pheromone peak and a simultaneous increase in the height of the alcohol peak were observed. The ratios of the pheromone peak height to alcohol peak height values were 93.0, 47.5, 15.5, 8.7, 4.0, 2.2, 1.77, after 1, 5, 9, 15, 30, 45, and 60 min, respectively. These results demonstrated an enzymatic hydrolysis of the pheromone to the alcohol. In a subsequent experiment, the relative percentage of pheromone converted by the antennae, haemolymph, and legs was 33.9, 10.1 and 6.5% per 60 min.

When the inhibitor, (Z)-7-dodecen-1-ol (final concentration 2.5×10^{-3} M), was incubated with antennal supernatant (100 µg protein ml.$^{-1}$), it produced a rapid initial positive increase in absorbance which gradually declined to a negative value during the first 5 min, after which a plateau was reached that was stable for over 1 h (Fig. 1e). Addition of more inhibitor caused another, but slower, positive increase in absorbance change. This response, by contrast to that obtained with the pheromone (Fig. 1e), suggested that the absorbance change was due to reversible conformational transitions in proteins binding the alcohol as noted by M. Laskowski[13]. Incubation of the antennal preparation (100 µg protein) with the inhibitor (1.3×10^{-3} M) for 15 min before addition of the pheromone (1.3×10^{-3} M) did not prevent the absorbance change induced by the pheromone.

The significance of the in vitro conversion of the pheromone

to inhibitor in the mechanism of olfaction by this insect remains obscure. There is no direct indication that this reaction is related to transduction[1]. It is possible, however, that enzymatic hydrolysis of the pheromone to the alcohol is a mechanism which regulates adaptation in the neurone and/or is a means of biologically inactivating the pheromone to prepare the dendritic receptor membrane for subsequent stimulation. This reaction may also be useful in obtaining inhibitors in other species whose mating behaviour is mediated through pheromones.

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Morphogenesis and Regulation in Spite of Continued Mitotic Inhibition in *Xenopus* Embryos

THERE is evidence that the development of pre-patterns in vertebrate embryos involves not the counting of the cells but the erection of a "map" of information whereby zones of space are devoted to development of particular differentiations by cells within them. Thus in amphibian neurulae following initial removal of much of the totipotent blastula, abnormally few cells create a whole pattern, although each cell has normal dimensions. Conversely, in normal-sized *Xenopus* embryos having haploid cells, an appropriately larger-than-normal number of these smaller cells is assigned to each somite, the somite blocks being normal in number and dimensions[1].

Table 1 Inhibition of Cellular Multiplication during *Xenopus* Morphogenesis

Experiment	Controls at stage of operation	Cell number/embryo (without yolky endoderm) (s.e. in parentheses)			
		Control		Blocked at operation	
		Stage 14/15	Stage 22	Stage 14/15	Stage 22
I, Block with colcemid	4,300 (300) (stage 10+)	17,800 (500)	30,600 (400)	4,600 (300)	4,700 (300)
II, Block with mitomycin C and colcemid	5,700 (400) (stage 10½)	18,200 (400)	28,900 (500)	6,500 mitomycin (300) 5,600 colcemid (300)	6,200 mitomycin (300) 5,900 colcemid (300)

Cell numbers are the averaged results of counting four haemocytometer samples from each of two cell suspensions made with synchronous pairs of embryos at the morphological stages described. They are given, together with their standard errors, to the nearest 100 cells.

It has been suggested[2] that the cell cycle is necessary to normal development in other ways, either for the adjustment of cells' developmental tendencies in response to regulative changes in the pre-pattern of "map" or else as part of the ongoing process of cell commitment and histodifferentiation itself.
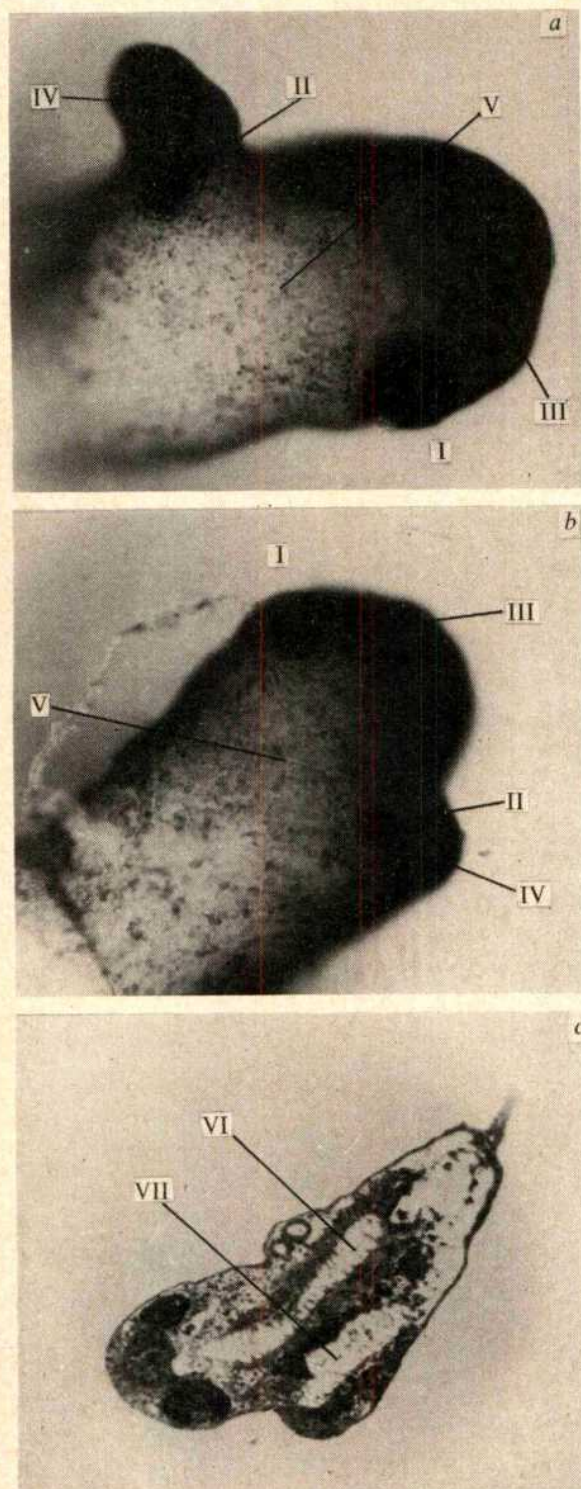
Fig. 1 a and b, Ventrolateral views of living embryos at about stage 25, following operations at stage 10 when additional head organizers were implanted. a, Control; b, cell cycle blocked with mitomycin C from time of operation; c, horizontal section of operated embryo at about stage 27, colcemid blocked, showing dual axial structure most readily seen in the paired, histodifferentiated notochord. I, Host cement glands (mouth precursor regions); II, cement glands of secondary inductions; III, forebrain fields of hosts; IV, forebrain fields of secondary inductions; V, equivalent regions, for visual comparison of average surface cell diameter; VI, host, and VII, secondary notochord, both showing histodifferentiation.

Recent work in an insect system[3] suggests that the first of these situations applies there.

Opportunity to test further the relation of cell number and an ongoing cell cycle to at least the early phases of amphibian differentiation has been provided by my finding that cell division in beginning gastrulae may be entirely inhibited, either with colcemid or with mitomycin C, and that this is followed by essentially normal development up to early tailbud stages. Cell counting has also shown that mitosis is arrested within a time, from application of the drugs, short relative to the normal cell cycle time in gastrulae. Gastrulation and neurulation movements are unaffected by mitomycin C, which is believed to cause intra-chromatid crosslinkage of DNA, preventing subsequent rounds of chromosomal replication without necessarily rendering chromosomes abnormal as RNA templates[4]. The movements are significantly slowed, although normal, under colcemid, a finding not surprising in view of the suspected involvement of microtubule systems in embryonic cell movements.

At stage 10[+] (ref. 5), the early gastrula subjected to mitotic inhibition in these experiments, almost all the territories of amphibian embryos are developmentally labile and pluripotent[6]. By late neurula stages cells are specialized in morphology and activity, and probably[7] in RNA transcriptional patterns, so the finding with colcemid has seemed startling in view of the condensed state of chromosomes as held in metaphase arrest. Histology shows, however, that in spite of permanent absence of mitoses, these nuclei return after some hours to an interphase-like configuration, having the nucleoli normal to postgastrular stages.

By late neurula stage 22, some 12 h after the blockage of mitosis, differentiation potency within the mesoderm and overlying, induced nervous system has become broadly restricted according to cell position[6]. The normal cell number at this stage is some 7 or 8 times that found in the early gastrula and in the inhibited embryos, representing some three cell generations. Thus the cell diameter difference of approximately 2 to 1 found along the dimensions of their structures in histological sections is as expected.

Table 1 shows results, in experiments on two separate batches of eggs, of cell counting following inhibition of cytokinesis. Details of handling of embryos, and of the operation mentioned below, are presented elsewhere[8]. Demembranated embryos were placed at stages 10[+] or 10½[+] (ref. 5) on a 2% 'Agarose' bed in one-third strength Holtfreter solution (pH 7.2) containing either 0.05% colcemid (CIBA) or 40 γ ml.[-1] mitomycin C (Sigma, London). The blastocoel was gently flushed by micropipette, through a small rent made animally, ensuring access to all cells by the drug, After 45 min, with the rent fully healed, embryos were transferred to one-tenth strength Holtfreter, on glass, containing a holding concentration of either 0.015% colcemid or 20 γ ml.[-1] mitomycin C. Controls were similarly treated without exposure to antimitotic agents.

Pairs of embryos at the stages shown were placed in Ca^{2+} Mg^{2+} free Holtfreter with EDTA 150 mg l.[-1] (pH 8.2) for cell-counting. The large, yolky vegetal cells of early gastrulae, or their well known derivatives in later stages, were rapidly dissected free and discarded, as their variable size and fragility rendered accurate cell-counting difficult. Each pair of embryos was then transferred into 0.3 ml. of the same medium and gently pipetted to a single-cell suspension.

The results shown are typical of those in several further experiments. Cell division is effectively abolished in embryos blocked by both these agents. There is no evidence for breakaway from the block between stages 14–15 and stage 22, after which cell-counting by the direct method used is impossible because of histodifferentiation and matrix secretion. In each of six experiments employing direct cell-counting, however, no mitoses have been observed histologically in parallel blocked material at stages 26–27, some 4 h later, when notochord vacuolation, muscle-cell striation and spontaneous twitching have developed.

By performing a classical operation upon gastrulae, simultaneously blocking the cell cycle as described, I have tested the proposition that cells must traverse some part of the normal cell cycle, in order to respond appropriately to information assigning them to a changed position in a pre-pattern. An additional stage 10 dorsal blastoporal lip is implanted into a host early gastrula at a wide angle from its own organizer[8]. In such circumstances, a secondary anterior pattern of differentiation tendency and inductive activity is induced, leading by neurula stages to a double axial structure anteriorly, fusing to a single one posteriorly. Vital staining of implanted organizers shows that most of the new pattern extends over host cells.

Fig. 1 shows stage 25 embryos following such operations, with their dual anterior axial structure. Cell counting during this experiment showed a 7.5 : 1 cell-number ratio between control and blocked operated embryos by stage 22. The histological appearance of such a double set of axial structures, at stage 27 in a colcemid blocked embryo, is also shown. Counting data show that the cell cycle must be inhibited, following imposition of the drugs, well within the half hour taken by the graft to achieve normal cell contacts with host material.

Anatomical results of these operations are entirely similar over a series of some fifteen control, colcemid inhibited, and mitomycin C inhibited embryos in three experiments, where cell number appropriate to controls at time of operation is still observed at stage 22 among the operated embryos themselves.

Thus such differentiation as expressed in normal morphogenesis by tailbud stages, including the functional histodifferentiation seen in muscle and notochord, has developed in the absence of mitosis or of normal chromosomal replication. Further, such inhibited cells have altered their fate and final committed state appropriately upon becoming part of a new morphogenetic field. These results tell nothing, however, about the nature of the information constituting such fields[9].

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Ultrastructure of Synaptic Vesicle Formation in Cerebral Cortex

SYNAPTIC vesicles have assumed a role of singular importance in models of synaptic function as morphological evidence of their existence appeared simultaneously with the "quantal" theory of transmitter release[1]. The problem of synaptic vesicle origin, essential to understanding this role, has led to extensive investigations. Electron microscopic studies[2-4] have demonstrated synaptic vesicles attached to the axolemma or open to the extracellular space, and suggest that some synaptic vesicles form by a process of micropinocytosis at the presynaptic terminal membrane. Freeze-etched preparations, besides show-
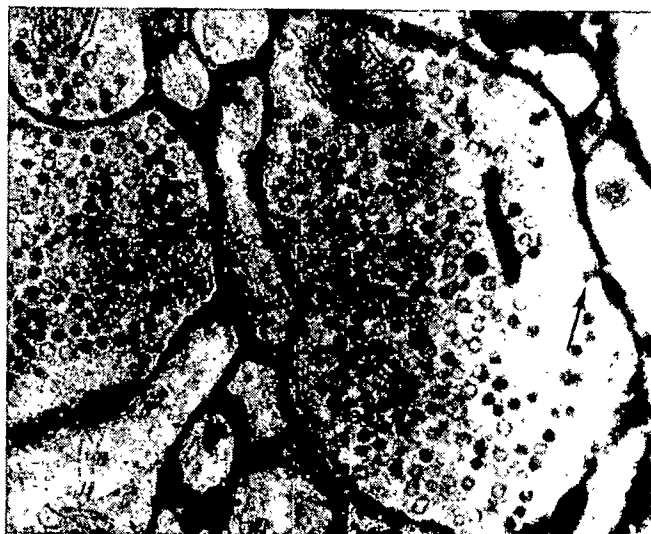
Fig. 1 Cortex extracellular space is filled with electron dense reaction product of horseradish peroxidase (HRP) 1 h after subarachnoid application. Presynaptic terminals show many of their synaptic vesicles filled with tracer and two vesicles (arrows) are intimately associated with the plasmalemma. ×53,000.

ing smaller micropits (synaptopores) at presynaptic sites, have shown similar plasmalemmal vesicles at non-synaptic sites[5]. A micropinocytotic origin of synaptic vesicles remains uncertain, however, and other workers suggest an intracytoplasmic mechanism of origin[6,7].

Electron dense protein tracer techniques make it possible to study communicating events between the extracellular space and intracellular structures and to bypass the brain barrier system[8]. Here we investigate the relationship between synaptic vesicles and the extracellular space in mammalian neocortex using horseradish peroxidase (HRP) applied directly as a tracer. We show electron microscopic evidence of remarkable labelling of synaptic vesicles and frequent loading of "coated" pits with peroxidase at the presynaptic terminal membrane.

Similar results were obtained from ten rabbits, two cats, and one monkey using either of two methods performed separately under halothane anaesthesia. In the first the subarachnoid space was exposed by a 10 mm craniectomy with a plastic ring attached to the surrounding bone creating a well to hold the HRP.

In the second a 27 gauge needle was inserted through the intact dura into the interhemispheric subarachnoid space for HRP injection. Approximately 20 mg of HRP (type II, specific activity, RZ 1.9 of possible RZ 3, Sigma Chemical Co., St Louis) in 0.5 ml. Ringer solution was injected within 30 min. The Ringer solution contained 147 mE Na, 4 mE K, 4.5 mE Ca, and 156 mE Cl (pH 5.2) and was allowed to reach room temperature (24° C) before injection. The injection technique was better for tissue preservation but HRP dispersion was less controllable. Tissue was fixed by intravascular perfusion of aldehyde fixative[9] at various times from 15 min to 4 h after HRP placement. Cortex treated in an identical manner, but without introducing HRP, served as a control. Tissue blocks were excised sharply and 50 µm sections cut with a 'Sorvall' tissue sectioner. Sections were incubated for 30 min in a solution containing hydrogen peroxide and 3,3′-diaminobenzidine[10], postfixed with osmium, and stained with uranyl acetate *en bloc*[11]. After routine dehydration and embedding, thin sections, unstained or stained with lead citrate, were studied on a 'Philips 300' electron microscope.

Within the area of HRP dispersion there was uniform flooding of the extracellular space with tracer. Almost all presynaptic terminals had labelled vesicles, many with as much as 80% of their vesicles containing HRP tracer (Figs. 1 and 2). These vesicles which were 300-500 Å in size, bounded by a trilaminar limiting membrane and dispersed among similar,

but electron lucent vesicles, appeared indistinguishable from synaptic vesicles. Tracer was contained within vesicles or occasional tubular structures (Fig. 1), but not free in the cytoplasm, indicating the vesicles were loaded prior to fixation[12]. A survey of micrographs revealed no tracer in sectioned axons.

Invaginations of various depths and configurations from shallow depressions to deeper bell-shaped and U-shaped profiles in the plasmalemma of presynaptic terminals are shown in Fig. 3. These "pits" were loaded with HRP tracer and, although not specifically stained to show a peripheral structure, they generally appeared to be coated (Figs. 2 and 3). They were apparently constricted at their base forming a spherical vesicle resting on a small cone of plasmalemma (Fig. 3d), and were able to separate, becoming interspersed among other vesicles in the terminal. Microinvaginations were appreciably more frequent at non-synaptic sites. Occasional microinvaginations (less than 2%) could be identified directly opposite the postsynaptic density but another group (approximately 20%) appeared to border the synaptic cleft and the remainder were found at non-synaptic sites. The sequence of images shown in Fig. 3 suggests that "coated" vesicles, previously described in presynaptic terminals[2,13], communicate with the extracellular space where they become filled with tracer during the process of micropinocytosis. It is possible that HRP-loaded "coated" vesicles may explain the many labelled synaptic vesicles in these experiments[13]. These observations could support the theory that some synaptic vesicles form by microinvagination of the plasmalemma.

Variability in the number of labelled vesicles among different terminals, both in time and location, was observed, but not yet quantified. Experiments at the neuromuscular junction indicated that resting synapses show little peroxidase uptake while stimulated preparations show many HRP containing
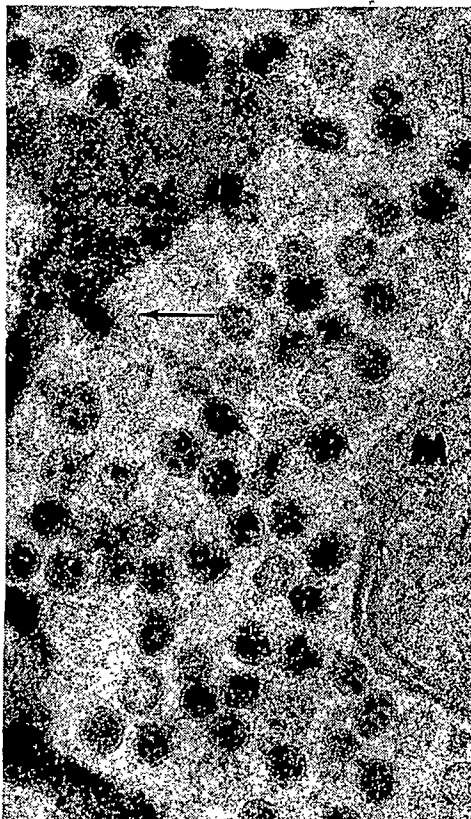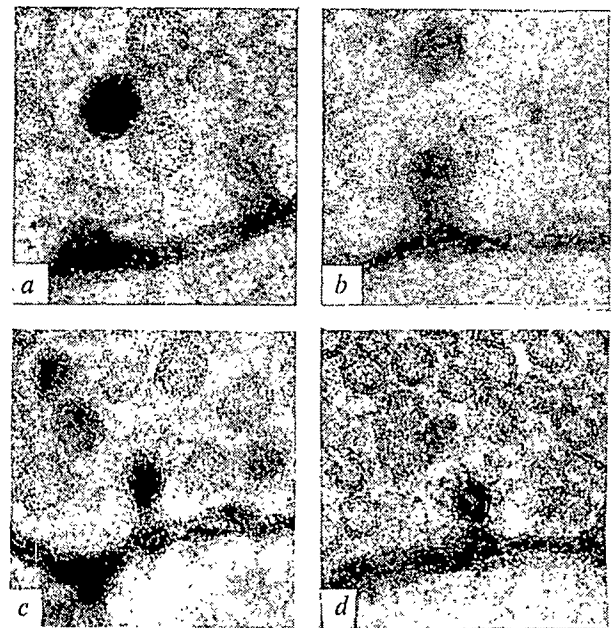
Fig. 3 Images consistent with micropinocytosis at presynaptic terminals from different animals. Four degrees of association shown between the "coated" pits and the plasmalemma. a, Tracer fills a shallow invagination in the plasmalemma of the presynaptic terminal. ×150,000. b, The membrane of this tracer filled "coated" pit is in continuity with the plasma membrane, allowing communication with the extracellular space through a large neck. ×165,000. c, The membrane connecting this "coated" vesicle and the plasmalemma has constricted, leaving only a thin channel between the loaded vesicle and the extracellular space. ×140,000. d, This HRP loaded "coated" vesicle appears resting on a cone of plasmalemma and may be in the process of losing contact with the axolemma. ×150,000.

vesicles[14,15]. No specific attempt at synaptic stimulation was made during our experiment, although the experimental conditions could have stimulated local increased synaptic activity to account for the labelling. In this case, the HRP present in terminals could be an indicator of synaptic activity during the observation period.

Our findings suggest that frequent communication between the extracellular space and synaptic vesicles occurs, and support the theory that this is accomplished through a mechanism of micropinocytosis by "coated" pits and vesicles. Whether there is any difference in direction (that is, discharging or loading) between invaginations adjacent to the synaptic cleft or elsewhere on the terminal remains unknown and is a limitation of this cytochemical tracer technique. Endocytosis appears to be an important property of presynaptic terminal surface membrane as well as surface membrane of the perikaryon[16], although the controlling conditions are as yet unknown. Endocytosis may play an important role in synaptic function; but this may or may not be immediately related to synaptic transmission[17].

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Fig. 2 An axon terminal containing many vesicles labelled with extracellular tracer. A mitochondrium (m) is present. Several labelled vesicles (*) are clustered near the tangentially sectioned plasmalemma and a "coated" vesicle (arrow) appears fused with the plasma membrane. ×106,000.

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Fig. 1 Effects of anticholinergic drugs on severity of withdrawal from morphine. The narcotic was withheld from 17 rats tolerant to high doses of morphine sulphate (see text) by substituting saline injections for the regular morphine injection in all the rats at 0 h. Withdrawal severity was assessed by scoring, on a discrete scale of from 0-5 points, the following behavioural signs: piloerection; shrieking and escaping upon gentle handling; shrieking and attacking upon being poked with a needle; startle response to a puff of air on neck or haunches; hunch-backed posture; territorial exploring; apparently non-purposive motor hyperactivity ("restlessness"); muscle twitches; body tremor. Severity of the total withdrawal syndrome was quantitated by finding the average total score of all signs per animal for each group of rats over any given check period. Such averages are represented by heights of the vertical bars. Open bars represent withdrawal severity for rats which received saline injections (controls, 5 rats); hatched bars represent that for treatment with mecamylamine hydrochloride 6.0 mg kg^{-1} (6 rats); shaded bars that for treatment with a combination of mecamylamine hydrochloride 6.0 mg kg^{-1} with atropine sulphate 4.0 mg kg^{-1} (6 rats). Drugs were injected at times indicated under arrows. Vertical lines represent standard errors; horizontal lines joining bars indicate significant ($P < 0.05$) differences between the scores.

Morphine Withdrawal Syndrome Responses to Cholinergic Antagonists and to a Partial Cholinergic Agonist

MORPHINE impairs the release of acetylcholine (ACh) at muscarinic and nicotinic sites in the periphery[1-3], and within the brain[4-8]. Paton[9] suggested that morphine's ability to impair ACh release might be the origin of the morphine withdrawal reaction. He proposed that ACh could accumulate within cholinergic terminals during habituation to the narcotic and then flood out onto cholinoceptive tissues when the drug is withdrawn, giving rise to opiate withdrawal symptoms. He later[10] outlined the autonomic imbalance seen during narcotic abstinence, and suggested that supersensitivity might develop in cholinergic receptors during morphine habituation, as a result of the deprivation due to impaired release.

We have attempted to test the cholinergic hypothesis by administering drugs which act specifically on cholinoceptors to rats undergoing withdrawal from morphine. In one study seventeen male Sprague-Dawley rats (initially 100 g) were given morphine sulphate by i.p. injection twice daily; doses were increased regularly from 20 mg kg^{-1} per day up to 600 mg kg^{-1} per day over 21 days. The animals responded with a severe abstinence syndrome when the drug was withheld. Severity of the total withdrawal syndrome was assessed by scoring and then averaging the prominence of various behavioural signs of withdrawal upset (Fig. 1). A "blind" design was used; drugs, solutions and animals were all coded until after the study had been completed and the results analysed. Rats were divided into three groups during withdrawal and given i.p. injections of either saline (control group—5 rats) or one of two anticholinergic treatments (mecamylamine group—6 rats; atropine-mecamylamine combination group—6 rats) at various times during the withdrawal reaction (Fig. 1). Significance of the data was assessed by Student's *t*-test for unpaired data using the square-root scale transformation[11] to check the validity of inferences made from data consisting of small whole numbers with many zero results.

In the first check period after initial withdrawal from morphine (14-15 h) there were no significant differences in withdrawal severity between any of the three groups (Fig. 1). Withdrawal severity rose significantly in both groups of drug-treated rats after injection of the anticholinergic drugs at 22 h but the increase in the saline-treated group was not statistically significant. The atropine-mecamylamine mixture, however, reduced withdrawal severity when administered at 42 h after initial withdrawal; this may be seen by comparing scores for the saline- and mixture-treated animals during the 44-45 h check period. Withdrawal severity in both drug-treated groups but not controls was significantly less during the 49-50 h check, which followed injections at 48 h, than during the 44-45 h check. The effects of the 48 h injection seemed to wear off after 10 h, scores for drug-treated animals at 58-59 h being similar to controls in the same check period but consistently higher than scores for the drug-treated animals during the 49-50 h check.

There thus appears to be a biphasic response to anticholinergic treatment during withdrawal from morphine habituation. Collier, Francis and Schneider[12] have described similar results with atropine, chlorophenylalanine and indomethacin in morphine withdrawal precipitated by naloxone in rats. They observed, in individual signs of withdrawal upset, biphasic responses to all three agents and concluded that acetylcholine, 5-hydroxytryptamine and prostaglandin(s) are all involved in morphine withdrawal. A biphasic or even multiphasic response to anticholinergic treatment is predictable within a cholinergic mechanism, however, because it is unlikely that all synapses will recover at the same rate or be at the same stage of derangement at any given time during the withdrawal reaction. Adding a cholinergic antagonist early in the abstinence syndrome might therefore actually increase the deprivation of cholinergic activity at those synapses not yet effectively relieved of their morphine burden whilst, at fully-recovered synapses, not causing sufficient blockade to overcome excessive cholinergic stimulation.

Our own results suggested that withdrawal severity might be reduced throughout the entire syndrome by the administration of a drug which could prevent development of receptor supersensitivity during impairment of release but which could also antagonize cholinergic drive during periods of excess[28]. These criteria might be met by a partial cholinergic agonist. Choline chloride is a weak cholinergic agonist[13,15] which readily enters cells and passes the blood-brain barrier in spite of its quaternary nature[16-18]. An initial study on six morphine-habituated rats tested the effects of choline on withdrawal from morphine addiction. The effect of choline chloride on the severity of withdrawal is shown in Fig. 2. The treatment clearly diminished intensity of the withdrawal syndrome monitored over a 73 h period in comparison with the control addicted animals which were given saline injections only during withdrawal over the same period. Choline-treated animals suffered less weight loss, maintained normal grooming
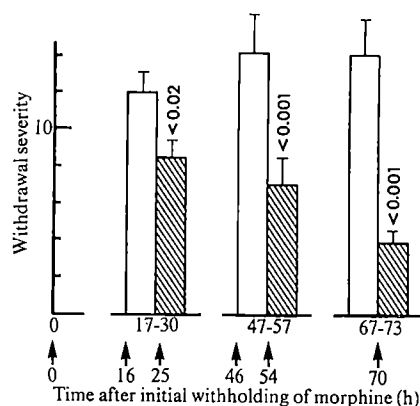
Fig. 2 Effects of choline chloride on severity of withdrawal from morphine. The narcotic was withheld from 6 rats tolerant to high doses of morphine (see text). Either choline chloride 100 mg kg⁻¹ (choline-treated group, 3 rats) or saline (control group, 3 rats) was substituted for the regular dose of morphine at 0 h. Withdrawal severity was assessed as described in caption to Fig. 1 except that additional scores were assigned for signs of salivation, erection and ejaculation while a negative score was assigned for grooming. Values for severity in the period 17–30 h are the mean of that observed in four individual check periods over that time; there were three individual check periods in each of the time periods 47–57 h and 67–73 h. The rats in both groups were reinjected with their initially-administered solutions at times indicated under arrows. Open bars: withdrawal severity in rats treated with saline injections during withdrawal (controls); shaded bars: that for rats treated with choline chloride. Vertical lines represent standard errors, significance of differences between scores for saline-treated and choline-treated groups indicated by P values above shaded bars.

and appeared in general to be normal healthy rats as compared with the saline-treated controls. The ameliorating effect of choline on withdrawal severity was not biphasic, by contrast with the results described here for cholinergic antagonists or for drugs interfering with other putative neurotransmitters[12]. Choline-treated rats showed less severity than controls in all ten of the individual check periods from which the data summarized in Fig. 2 were drawn.

Involvement of neurotransmitters other than ACh in the morphine withdrawal syndrome has been considered[12,19-22] but there is controversy over their importance[23-27]. Choline chloride, regardless of the possible involvement of non-cholinergic systems, appears to be very effective in treating the narcotic withdrawal syndrome in rats throughout a long period of monitoring. We explain this as due to a major involvement of a cholinergic mechanism in this syndrome and are seeking an optimal treatment in further studies on cholinergic systems altered by chronic administration of morphine.

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Comments on the "Isolation, Identification and Synthesis of a Specific-behaviour-inducing Brain Peptide"

DURING the past six years a remarkable series of publications has appeared, claiming the transfer of various specific learned behaviours from animal to animal by i.p. injection of extracts made from brains of trained donors. These are cited in the latest paper[1], in which Ungar and his colleagues propose an amino acid sequence for a pentadecapeptide isolated from the brains of donor rats trained to avoid a dark box. Injection of this material into untrained recipient mice is alleged to transfer the learned dark avoidance. The molecule has been named scotophobin, after the Greek words meaning "fear of the dark".

The long controversy over the claims for transfer of learned behaviours was reviewed by W. W. Stewart[2] in an article to which Ungar et al. replied[3]. Unfortunately, the Stewart review dealt very largely with the weakness of the claims for a particular amino acid sequence, while paying far too little attention to more crucial weaknesses at the heart of the interpretation. After all, some oligopeptide material has evidently been isolated from trained donor rats. If this material—whatever its exact structure or state of purity—is truly capable of specifically transferring a learned behaviour to untrained recipient animals, the discovery certainly ranks among the most fundamental in modern biology. It is because of the far-reaching implications that so much controversy has been aroused. For the same reason, it is of the utmost importance that the experimental

evidence be as complete and convincing as possible. I shall point out two major uncertainties about this work, which apply as surely to the present experiments with a peptide as to previous experiments with crude brain extracts.

The first question is: Can the investigators state precisely the conditions for carrying out an assay, in such detail that competent scientists elsewhere can reproduce their results? Our own repeated failure[4] could be written off as the bungling work of incompetents, were it not matched by published experiences of some others, as cited by Stewart[2] and by Ungar[3,4]. It would be interesting to find out how many tried and failed but did not feel such an outcome was worth publishing. Is Ungar's dictum, "Negative results are always easier to obtain than positive ones,"[4] really true? It has a strange ring to me, as a pharmacologist. Suppose we are told that the median analgesic dose of a new narcotic drug in a given strain of mice is 1 mg kg^{-1}, using the hot plate procedure with specified parameters of time and temperature. If the information is correct, it will certainly be harder, not easier, to find no analgesic activity at all, at sufficient doses. The truth is, by following the specified procedures, we can expect to confirm that the drug is an analgesic. One of the most disconcerting things that can happen to a scientist is the failure of other investigators to confirm his findings. Clearly, something is wrong, at the very least a failure to specify all the relevant conditions of the experiment. Such a situation calls for the most intensive effort to resolve the difficulty, and thereby to sharpen understanding of the relevant variables. It is hardly reasonable to find fault with others for not exploring all the variables that should have been worked out in the first place. It is universally agreed that reproducibility is a necessary condition for accepting the validity of a scientific finding.

The second question goes to the heart of the interpretations placed by Ungar upon his work. Let us accept, for the sake of argument, that the results are too difficult to obtain except in the expert hands of a few, but that they are none the less real. What then, has been shown, and what does it mean? To answer this, and to understand the crucial defects in Ungar's experimental design, one has to have seen or done these experiments oneself. In discussing "scotophobin", I shall discuss only those experiments employing dark avoidance, as this was the paradigm used in the isolation of the oligopeptide.

In Ungar's procedure[4] a donor rat is placed in a centrally placed, illuminated white box, which is connected by tunnels to another illuminated white box on one side, and to a dark box on the other. The rat follows a normal instinctive behaviour; it runs into the dark box. There it is given foot shock, and it runs out again. This animal, it should be noted, will rarely enter the dark box again spontaneously. Indeed, this is an example of the classical paradigm known as "one-trial learning", which has been used extensively by McGaugh[6] and others to study short- and long-term memory. If learning to avoid the dark box led to the production of a "memory transfer factor", it should be possible to prepare active extracts after such a single trial, in which a long-lasting aversive conditioning (dark avoidance) is established—if not immediately, then surely at some time later, when the memory has been consolidated. But Ungar knows and admits that this will not work. "In passive avoidance," he writes, "training is completed on the first day, but several more days are required for the brain to accumulate the excess of material necessary for transfer."[4]. This means several more days of training, not merely several days to accumulate the "excess of material necessary for transfer". In other words, there is an utter lack of temporal relationship between learning and consolidating the dark avoidance, on the one hand, and the appearance of the alleged transfer material, on the other.

What actually happens in the training of donor rats is this. After the animal is shocked and runs out of the dark box, the investigator has to sieze it, and force it through the tunnel into the dark box, where it is again shocked and runs out. This extraordinary stressful procedure is repeated five times in rapid succession, to complete the first day's training session. Ungar's description is: "If he does not run back (this is the rule after the second session), he is pushed through the gate into D and shocked. Each daily session consists of 5 shock periods of 5 s each, separated by intervals of 10 s"[4].

The next day, when the rat is first placed in the white box, it immediately shows fear. It cowers in a corner, defaecates, trembles, and often tries to leap out of the box. Again the investigator must seize the animal, which struggles vigorously and tries to bite, until it is pushed and twisted through the tunnel, locked into the dark box, then shocked and allowed to run out. Sometimes the rat behaves in a confused manner, "freezing" inside the dark box, and refusing to run out; then the investigator has to push it back through the tunnel into the white box. This whole procedure (five trials in succession) is repeated on six successive days. Then the animal is decapitated. Thus, donor rats receive massive stressful manipulation as well as shock at an intensity and for a duration far greater than required to learn dark avoidance.

If a naïve observer were to watch the training procedure without being told that dark avoidance was the objective, and if he were then told that brain extracts from such animals induced a behaviour different from that induced by brain extracts of untreated controls, he would certainly conclude that extreme stress was the causative agent. Any competent scientist would know that the proper control group should consist of rats that received equivalent foot shock and intensely stressful manipulation, without the dark box contingency, that is, with nothing to learn. But one looks in vain for data on even one such adequate control experiment in Ungar's work. The only published controls are found in a table[7], where a total of twenty donor rats were subjected to shock in a lighted chamber or white box. No further description of the experimental conditions is offered, and there is no intimation that these animals were subjected to stressful manipulations. Other than this, and despite the publication of at least seventeen articles on the subject, one finds only undocumented assertions about the specificity of transfer of dark avoidance, or very limited data on the specificity of transfer of behaviours other than dark avoidance.

During my visit to Houston, where I observed Ungar's techniques at first hand, I noted that although he was recording latency (that is, time required for a recipient mouse to first enter the dark box), all his published data concerned dark box time (that is, total time spent in the dark box in a 180 s trial). I thought this curious, because if dark avoidance behaviour were really induced by the injections, the latency should be increased. This is elementary logic. Indeed, latency is the common and accepted measure for such behavioural phenomena among experimental psychologists. Yet Ungar has never used latency, and has never claimed to have shown differences in it.

Dark box time, on the other hand, which is Ungar's standard measure, would probably be sensitive to other behavioural effects. A recipient mouse that wanders about more because it is hyperactive would naturally be more likely to leave the dark box than a more passive animal. Amphetamine, for example, might well reduce dark box time. A recipient mouse whose perception or interpretation of the environment had been obtunded would be more likely to leave the dark box than an alert animal. Morphine, for example, might well produce this effect.

Investigators who were seeking alternative explanations to their own preconceived ones would have performed some

of the elementary controls suggested by the remarks above. My own guess is that if there is a real effect at all, and if there is a natural or synthetic peptide producing decreased dark box time (not "dark avoidance"), it is probably a non-specific factor induced by stress. This, in itself, could be a discovery of some importance. But it serves no useful purpose to claim the isolation and synthesis of "the coded molecule involved in dark avoidance"[4] until three things have been done:

(1) The precise conditions for the transfer of "dark avoidance behaviour" by crude extracts should be written down in detail and followed by several investigators, to ascertain once and for all if the phenomenon meets the test of reproducibility.

(2) Crude brain extracts from stressed control donors should be shown to lack the capacity to induce dark avoidance. This experiment must, of course, be carried out in a blind design, concurrently with extracts from a trained donor group. Ideally, the extracts should be sent (after coding) to several groups of investigators for evaluation, as one might do in the preclinical testing of a new drug.

(3) The oligopeptide should be shown to be present in brains of trained donors and absent from brains of stressed untrained donors. The work-up of material from both sources should be concurrent, each batch of material should be coded and unknown to those engaged in the isolation, and several groups should carry out the procedure. Since more than 4,000 rats were required for the isolation of "scotophobin", it may suffice, as a first step, to show that the specified fractionation procedures that led to the isolation of the peptide will produce biologically active fractions with trained donor brains but not with stressed control brains.

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Ouabain Binding to the Sodium Pump

IN the course of studying ATP hydrolysis by the sodium pump, we have measured ouabain binding to ox brain microsomes. Our results on binding in the presence of Na, ATP and Mg agree with earlier findings, but our results with Mg alone lead us to question the validity of models which have been proposed for the mechanism of the sodium pump[1-3].

To ensure that equilibrium was reached between bound and free ouabain, the time course of binding was measured at a ouabain concentration of 5×10^{-8} M (see legend to Table 1). With either Na+ATP+Mg or Mg alone, a plateau was reached after about 45 min, and 60 min was kept as the incubation time in all further experiments. The level of ouabain binding

at equilibrium was the same with 5 mM MgCl$_2$, whether or not Na+ATP were added. A more stringent test was to determine the affinity (dissociation constant) and number of receptor sites for the reversible reaction

$$\text{enzyme.ouabain} \rightleftharpoons \text{enzyme} + \text{ouabain}$$
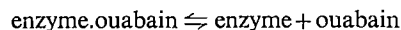
On raising the ouabain concentration (up to 2×10^{-7} M), there was more binding, of a kind that allowed a Scatchard[4] analysis of the results. The value for the dissociation constant with Na+ATP+Mg (Table 1) agrees with previous work[5], as does the turnover number, calculated from the number of binding sites. Table 1 shows, however, that the values for the dissociation constant and number of binding sites with Mg alone were not significantly different from those with Na+ATP+Mg. This result shows that the binding is quantitatively equivalent in the presence of either Na+ATP+Mg or Mg alone. Potassium inhibited the binding in both conditions equally, 10 mM being sufficient to reduce the binding to the low levels found in controls, to which no additions of Na, ATP or Mg were made. The binding reactions are not identical, however, because 100 mM sodium, the concentration employed in the Na+ATP +Mg condition, completely inhibited the binding with Mg. In previous work the binding with Mg alone has been stimulated by P$_i$, but there is conflict on whether the level reached is greater[2] than or less[1] than that with Na+ATP+Mg. We find no effect of P$_i$ (up to 10 mM) in the presence of Na+ATP +Mg, whereas with Mg alone it caused a small, though significant, stimulation (25%).

One feature of the present study is that 2 mM EGTA was added to all solutions in order to remove traces of adventitious calcium. Tests with and without EGTA were made of ATPase activity and binding. The results showed the same degree of binding although there was a three-fold increase in ATP hydrolysis (see Table 1).

The results lead to three conclusions. First, calcium does not influence ouabain binding at the very low concentrations which inhibit ATP hydrolysis. There is therefore no obligatory correlation between the rate of ATP hydrolysis and the magnitude of ouabain binding. The second conclusion follows; namely, the ouabain binding site is spatially separated from the site at which calcium acts. This is consistent with inhibition by calcium from inside cells and by ouabain from outside. The third conclusion is that Mg alone is sufficient to cause a conformational change such that ouabain can bind to the same extent as with Na+ATP+Mg. This simple requirement is not a feature of models which have been proposed relating ouabain binding to the conformational state of the pump[1-3]. Before ouabain can become bound, it is clear that a conformational change must take place. This has hitherto been held to occur following the formation of either a phosphorylated intermediate or an enzyme-substrate complex. Our results show that ouabain can become bound in conditions in which neither of these two reactions could have taken place. It

Table 1 Ouabain Binding to Ox Brain Microsomes

Additions (mM)			Dissociation constant ($M \times 10^{-8}$)	No. of binding sites (per mg protein $\times 10^{13}$)	No. of experiments
Na	ATP	Mg			
100	3	5	2.35 ± 1.38	4.1 ± 0.4	6
None	None	5	2.61 ± 0.77	4.1 ± 0.6	4

Ox brain microsomes, prepared and assayed as described previously[6], contained sodium-dependent ATPase activity (5.3 μmol P$_i$ liberated/mg protein per h), which was raised three-fold (to 15.7) when 2 mM EGTA was added. Ouabain binding was measured in a medium containing 2 mM EGTA, 20 mM imidazole-HCl (*p*H 7.6) and, as appropriate, 100 mM NaCl, 3 mM ATP, 5 mM MgCl$_2$ and ^{3}H-ouabain (NEN, New Boston, Massachusetts). After incubation at 37° C, small portions were cooled to 0° C and then centrifuged at 100,000g for 30 min. The pellets were resuspended in 5% aqueous 'Triton X-100', and the bound ouabain was assayed by liquid scintillation counting. The results are expressed as the mean ± standard deviation.

therefore remains to be proved which of the conformational states revealed by ouabain binding is directly related to the normal function of the pump.

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A New Hypothalamic Pathway to the Median Eminence Containing Neurophysin and its Hypertrophy in Sheep with Natural Scrapie

THE hypothalamus is linked to the pituitary by two anatomically distinct neuronal neurosecretory pathways. The first, the hypothalamo-distal neurohypophysial system, commonly termed the supraoptico-neurohypophysial system (SNHS), arises in the "magno-cellular" cell bodies of the supraoptic nuclei (SON) and the paraventricular nuclei (PVN), whence their large axons descend via the internal infundibular zone to the posterior pituitary (Fig. 1)[1,2]. This system is characterized immunochemically by the neurophysins, the specific carrier-proteins for vasopressin and oxytocin[3-6].

The second, the hypothalamo-proximal neurohypophysial system, originates in "parvicellular" cell bodies in the hypophysiotropic area (HTA) of the basal medial hypothalamus and its fine axons terminate in the external infundibular zone of the median eminence and pituitary stalk (Fig. 1b)[2,7-9]. This pathway, containing many catecholaminergic neurones[10,11], conveys the specific adenohypophysial hormone-releasing factors[12,13], which have no known specific carrier-protein[14].

We have evidence for another neurophysin-containing pathway arising in the SON and PVN, but proceeding only to the proximal neurohypophysis and terminating in the external infundibular zone of the median eminence-stalk. We have found that a neurophysin-like antigen associated with pressor activity is normally present in the external zone of the infundibulum in sheep in amounts and in a form very similar to those found in the adjoining internal zone of large longitudinal axons of the SNHS.

Many clinical signs of natural scrapie disease of sheep are compatible with a progressive and severe disturbance of hypothalamic and pituitary function[15,16]. Severe losses of neurones in the SON and PVN are associated with degenerative lesions in the neurohypophysis[17], and the loss of neurones in the SNHS was considered to offer an adequate explanation for the clinical disturbances of water and electrolyte intake[17].

Livett and Parry[6,18] used a cross-species reactive neurophysin antiserum[19] to demonstrate the precise cellular location of neurophysin (or a substance so similar antigenically as to be cross-reactive) in the SNHS of normal and scrapie sheep and have correlated these semi-quantitative observations of neurophysin content with vasopressin estimations using the method of Dekanski[20]. Their results confirm the histological findings of Beck, Daniel and Parry[17], and provide evidence of degeneration of the SNHS with severe vasopressin insufficiency in the later stages of natural scrapie.
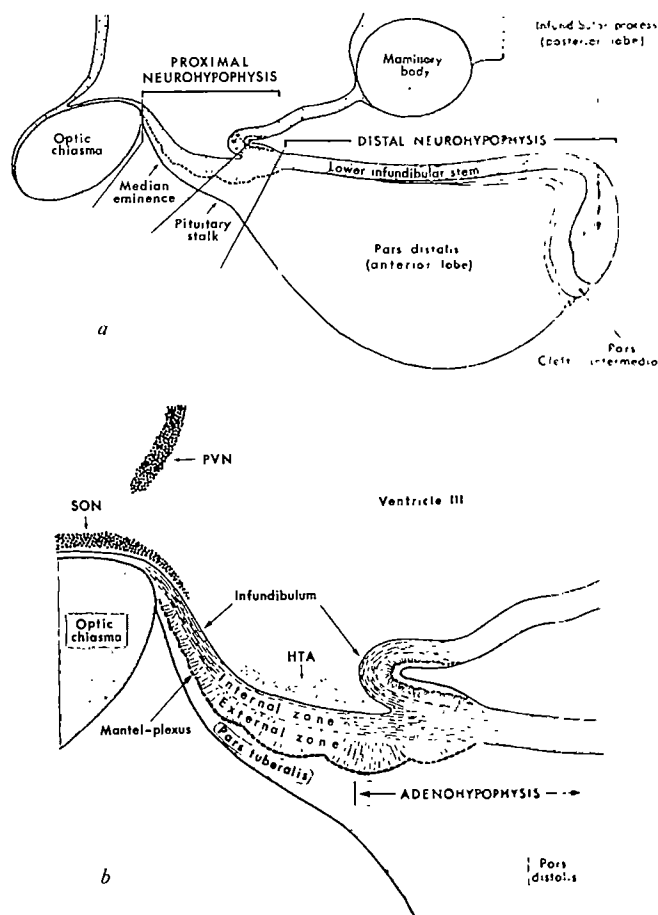
Fig. 1 *a*, Diagram showing the main components of the pituitary region in the sheep, as seen in the mid-sagittal plane. *b*, Part of *a* enlarged to show in greater detail the structure of the proximal neurohypophysis. Although this diagram represents a midline section through the cavity of the third ventricle, it indicates the approximate sites within the hypothalamus of the supraoptic nucleus (SON), the paraventricular nucleus (PVN) and the hypophysiotropic area (HTA).

On the other hand, the neurosecretory system sustaining what is presumably a neurophysin-vasopressin component in the external infundibular zone of the median eminence-stalk is preserved and is hypertrophic in scrapie sheep, showing a substantial increase of neurophysin immunofluorescence accompanied by an estimated two-fold increase in vasopressin content. The neurophysin fluorescence is particularly intense in the outer part of the external zone, where there is in the sheep an extremely dense network of short capillary loops[21], and also around the long portal vessels of the pars tuberalis, where it occurs frequently in the walls of the portal sinusoids. In the hypothalamus, however, no neurophysin immunofluorescence was observed except in the SON, PVN and in the intrahypothalamic tract originating from these nuclei.

Several considerations arise from these observations.

(1) We are not aware that neurophysin (or vasopressin) has been demonstrated previously in the external zone of the infundibulum[22,23], where the Gomori reaction for neurosecretion is usually negative in normal mammals[2], except the horse[24]. The external infundibular zone comprises the nerve terminals of the tubero-infundibular tract[2], the majority of which arise in the arcuate nucleus and contain dopamine[10,11], but with some containing noradrenaline[25] and some 5-hydroxytryptamine[26,27], while terminals of small axons from the SNHS occur in some mammals[28,29] and in birds[30].

(2) As specific neurophysin immunofluorescence occurred only in the SON and PVN neurones, we consider that there is in the sheep a tract from these nuclei running with the main tract of the SNHS caudally as far as the anterior (rostral) lip

of the entrance area of the infundibulum where it sweeps ventrally and outwards to terminate in the external infundibular zone and the Mantel-plexus, thus constituting a supra-optico-infundibular tract.

(3) The neurone populations of the SON and PVN are not anatomically and physiologically homogeneous, although characterized by intense specific neurophysin immunofluorescence.

(i) While the SON cell bodies are mostly magnocellular (MC), in the PVN there are a proportion, probably 25–30%, of parvicellular (PC) cells interspersed amongst the MC cells in the rat[31] and sheep[32 -34].

(ii) After permanent interruption of the tract from these nuclei to the infundibular process at the level of the lower infundibular stem, e.g. as in posterior pituitary lobectomy, 40–50% of all SON and 33% of all PVN neurones survive[35]. If the interruption is more proximal in the mid-pituitary stalk, for example as in low stalk section and intrasellar hypophysectomy, the loss of neuronal cell bodies is greater, and only 25–30% of the MC cells of both nuclei survive in the dog[36] and rat[31], while the PC cells of the PVN remain unaffected[31].

(iii) When the level of axon interruption is more rostral and anterior to the stalk in the median eminence–infundibular area of the ventro-medial hypothalamus, the loss of neurones is increased to 80–85%, especially in the PVN, in the dog[36], the goat[37] and man[38], suggesting that a further leash of axons, with cell bodies mainly in the PVN, has been severed.

(iv) After axon interruption at levels (ii) and (iii) new "miniature" neural lobes form from the proximal stump by outgrowth of new nerve fibres, which become filled with neurosecretory material[9,39,40]. The more rostral the stump the smaller is the new neural lobe[35,41].

(v) Two fibre pathways from the PVN to the neurohypophysis are recognized[42]: (a) a rostral tractus paraventricularis cinereus[43,44] joining the main supraoptico-neurohypophysial tract to the posterior pituitary; and (b) a more caudal and medial direct paraventriculo-hypophysial (infundibular) tract in the dog[45], the rat[31] and the rabbit[46] intermingling with the main tract in the caudal median eminence–infundibular entrance area and probably terminating in the outer layers of the median eminence-stalk[47,48]. The rostral pathway is thought to control vasopressin release, with the caudal one concerned with oxytocin release[49].

(vi) When recording from single neurones of the PVN following antidromic stimulation from the neural lobe, Cross, Novin and Sundsten[50] found that only about half the PVN neurones recorded could be activated from the neural lobe and concluded that "a large portion of PVN neurones may not project to the neural lobe".

There is thus considerable evidence for neurone populations in the PVN, and possibly also in the SON, which do not project to the posterior pituitary, and are available for a supraoptico-infundibular neurophysin pathway, arising mainly in the PVN and proceeding via the medial paraventriculo-infundibular tract of Laqueur to terminate in the external zone of the infundibulum.

(4) The neurosecretory axons innervating the median eminence may therefore consist of at least two subsystems, with the supraoptico-infundibular subsystem distinct from the main tubero-infundibular subsystem. Ultrastructural studies of the median eminence of the rat[48], the mouse[51] and mammals[52], and the toad[53], show a variety of nerve fibres and axon terminals containing at least three types of granules as well as vesicles, compatible with the neuronal and functional heterogeneity one might expect with two subsystems.

(5) The increased neurosecretory material in the external infundibular zone of scrapie-affected sheep[6] probably lies within this supraoptico-infundibular subsystem. After bilateral adrenalectomy[54-57] and hypophysectomy[58], similar neurosecretory material also accumulates in the external zone, often in new fibre outgrowths from the internal zone[54], with an increased content of corticotrophin-releasing factor (CRF) in the median eminence-stalk[59]. This accumulation may be reduced markedly by cortisone therapy[60], suggesting that the amount of stainable Gomori-positive neurosecretory material in the external infundibular zone and its CRF content reflect adrenal function.

(6) The role of the vasopressin-neurophysin complex in the external zone of the infundibulum is unknown, but its presence could provide a basis for the view that vasopressin is an adreno-hypophysial hormone-releasing factor, especially for adreno-corticotrophic hormone (ACTH)[14,60-62], and possibly concerned with the quick systemic component of ACTH release[52,63,64].

(7) In natural scrapie the supraoptico-infundibular neurosecretory subsystem is preserved and undergoes a functional hypertrophy in the terminal stages of the disease, probably related to the progressive loss of the principal vasopressin-oxytocin neurosecretory pathway to the posterior pituitary, and to the disturbances of adrenal function[16].

Natural scrapie in our sheep population behaves as an hereditary disease controlled by an autosomal Mendelian recessive gene with full penetrance[16,65-67]. As we now have sheep populations of the three scrapie genotypes[66], the discovery of the neurophysin-vasopressin pathway to the proximal neurohypophysis and of the divergent action of the scrapie genome on this pathway compared with that to the distal neurohypophysis offers another model for hypothalamo-neurohypophysial studies.

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Physicochemical Aspects of the Action of General Anaesthetics

THE physicochemical aspects of the action of anaesthetics have been studied for many years, with general agreement on the following conclusions. No chemical reaction seems to take place as in the extreme case of rare gases anaesthesia can be realized under proper conditions[1]. Observations favour the

membrane as the site of anaesthetic action[2], and the anaesthetic receptor seems to be of finite size and the anaesthetic agents molecules of limited size. It has been suggested that narcosis occurs when a critical fraction of space in the membrane is occupied by the volatile anaesthetic agent and it is generally agreed that narcosis is due to physical rather than chemical action of the molecule[3]. Relatively weak physical forces are involved and these are frequently thought to be associated with the London dispersion force[4]. Not surprisingly there is good correlation between anaesthetic potency and molar refraction[5], polarizability of the anaesthetic agent[6], molal volume, solubility in olive oil[7-10], boiling points, and other properties of the molecules that are decided by the relatively weak long range interactions. Correlation of anaesthetic activity with the van der Waals a and b constants[11] is of particular interest here. The constant a is associated with the cohesive forces between molecules, and b with their volumes. The qualitative correlation of the van der Waals constants with anaesthetic potency has been discussed by Wulf and Featherstone[11]. Wilson *et al.*[12] demonstrated the correspondence between isonarcotic pressure of inert gases and increased hydrolysis of choline esters expressed as a function of $\sqrt{a}$.

Here we examine the correlation between anaesthetic potency of molecules and the van der Waals a constant in somewhat greater detail than has been done previously. We chose this parameter as it reflects the cohesiveness of the molecule and correlations with it presumably would reflect the interaction of the anaesthetic molecule with the receptor site. In Fig. 1 we plot the best value of the logarithm of the anaesthetic pressure producing loss of righting reflex in mice against $\sqrt{a}$. One of the difficulties in making such a plot is that no one laboratory has measured all the relative anaesthetic pressures; consequently, the various values used come from many sources. In Fig. 1 we use the values of Smith[13], who studied the pressures for the loss of righting reflex in mice reported by many sources and arrived at a "best" value. The plot in Fig. 1 is interesting because if He is included it gives a linear relation to within experimental error between log P_{an} versus $\sqrt{a}$ for about five orders of magnitude. We have omitted strongly hydrogen bonding anaesthetics and completely fluorinated compounds (although SF_6 is included to illustrate its marked deviation from the linear relation) and limited ourselves to agents that may be expected to form near ideal solutions.
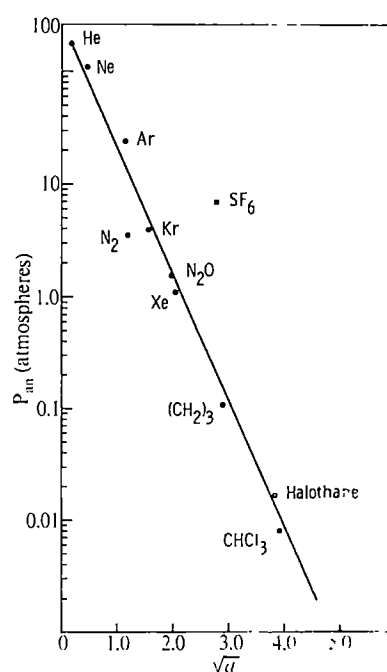
Fig. 1 Isonarcotic pressure in atmospheres plotted against the square root of the van der Waals a constant for various anaesthetics.

In a molecule such as SF_6 there is a large difference in the electronegativity of the fluorine and the central atom resulting in an excess of negative charge on the periphery. If the receptor site carries a negative charge, it would attract the SF_6 molecule with an affinity less than one would expect from the value of the molecule's van der Waals constant a. It is surprising that such a complex system appears to be described by a relatively simple function and this might be because there are compensating parameters involved.

We tested a working model of the anaesthetic-receptor system to see if it could provide us with a rationale of the correlation between $\log P_{an}$ and $\sqrt{a}$ as follows. When a nerve is excited, there is a large transient increase in Na^+ permeability of the fibre membrane, followed by a large transient increase of K^+ permeability. It is believed that the flow of ions takes place through aqueous channels[3] in the membrane which are opened or closed by an uncertain mechanism. When an anaesthetic dissolves in the membrane it expands which may reduce the size of any aqueous channels and so impede the flow of ions that anaesthesia occurs.

When anaesthetic molecules distribute themselves between the aqueous extracellular region and the membrane, the free energy change can be represented by

$$\Delta F = RT \ln \frac{C_1}{C_2} \quad \text{or} \quad \frac{C_1}{C_2} = \exp \frac{\Delta F}{(RT)} \quad (1)$$

where C_1 and C_2 are the anaesthetic concentration in the membrane and in the solution respectively, ΔF is the free energy change associated with the process and R is the gas constant and T the absolute temperature. When C_1 reaches a certain critical value, we assume that anaesthesia results. We will associate the dispersion energy with the free energy change in equation (1). It has been shown by London and others[14] that two neutral molecules interact with each other and this electronic dispersion energy is given by

$$W = -\frac{3}{2} \frac{\alpha_1 \alpha_2}{r^6} \frac{E_1 E_2}{(E_1 + E_2)} \quad (2)$$

or for identical molecules

$$W = -\frac{3}{4} \frac{\alpha^2 E}{r^6}$$

α_1 and α_2 are the electric polarizabilities of the two molecules, r is the distances between their centres and E_1 and E_2 are their effective electronic excitation energies. Slater and Kirkwood[15] pointed out that the latter expression should be multiplied by $\sqrt{s}$ where s is the number of coupled oscillators contributing to the interaction.

Next we establish a relation between the van der Waals a constant and the polarizability α, by comparing the virial equation of state of a gas with the expanded van der Waals equation giving the following expression for the second virial coefficient

$$K_2 = b - \frac{a}{NKT} \quad (3)$$

Now when the interaction energy of a pair of molecules at a distance r apart is $-B/r^6$ when $r > r_0$ and infinite when $r < r_0$ the second virial coefficient can be shown to be

$$K_2 = \frac{2\pi N r_0^3}{3}\left(1 - \frac{B}{kTr_0^6}\right) \quad (4)$$

By comparing the two expressions for K_2 and incorporating the dispersion energy for two like molecules from (2) we get the following expression for a

$$a = \frac{1}{2} \frac{\pi N^2}{r_0^3} E\alpha^2 \sqrt{s} \quad (5)$$

If this relation is substituted into (2) and then the result incorporated into (1) one gets

$$C_1 = C_2 \exp - \left[\frac{3}{2}\frac{(a)^{\frac{1}{2}}}{RT}\frac{\alpha_2}{r^6}\left(\frac{E_1 E_2}{E_1 + E_2}\right)\left(\frac{2r_0^3}{\pi N^2 E_1 \sqrt{s}}\right)^{\frac{1}{2}}\right] \quad (6)$$

We do not imply that this equation gives an accurate distribution of the anaesthetic molecules between phases, but it is hoped that it does give a qualitative indication of the parameters that decide this distribution. It is clear from this equation that one should expect a linear $\log C_1$ against $\sqrt{a}$ dependence if the other terms in the exponential expression are approximately constant. Part of this approximate constancy is compensatory. For example, as an anaesthetic molecule increases in size, the term r_0 in the numerator of the exponential factor increases but as the $\sqrt{s}$ in the denominator also tends to increase there is a tendency to compensate this. In addition, the excitation energies do not change greatly as one goes from one anaesthetic molecule to another. The strongest dependence in the exponential factor is the r^{-6} term. A possible rationale for the apparent constancy of this term is that in essence r is decided by the size of the receptor site (either an aqueous channel or a cavity formed by a carrier molecule). A small atom like He residing in a membrane site will have the same r value as a larger atom such as xenon since the distance from the centre of the atom to interacting points will be about the same in both cases. Finally, one should note the temperature dependence; and in this connexion, it is interesting to note that when the squid giant axon is lightly narcotized with ethanol, the height of the action potential is reduced and that this reduction can be restored by cooling[16].

The work of Johnson and Bangham[17] on the temperature dependence of the effect of anaesthetic agents on K^+ permeability in a model membrane and the studies of Johnson and Miller[18] on the antagonism of pressure in anaesthesia are also compatible with conclusions reached in this work. We conclude, therefore, that the correlation of log of anaesthetic pressure against $\sqrt{a}$ has a sound thermodynamic basis and may express a general principle of narcosis by chemically inert materials.

We thank Professor D. Benson for helpful discussions and encouragement.

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BOOK REVIEWS

The Sixteen Faces of Leo Szilard

The Collected Works of Leo Szilard. Scientific Papers. Edited by Bernard T. Feld and Gertrud Weiss Szilard. Pp. xxii+737. (MIT: London and Cambridge, Massachusetts, September 1972.) $17.50.

THE dust cover of the first volume of the *Collected Works of Leo Szilard* shows sixteen photographs of Szilard, each presenting a different facial expression. These sixteen faces could match the different facets of Szilard's activities. In this age of high specialization, when any one scientist can push forward the frontiers of knowledge only in a tiny sector, it is extremely rare to find a person who encompassed and moulded such a wide range of subjects. But then Szilard would have been a remarkable personality at any period of time. His fields of interest were physics, biology, sociology and technology, and to each of these he brought in refreshingly new concepts and a highly original approach. He was an inventor and an innovator, a path-finder and prognosticator, but he did not create a school, because he was too much of an individualist and a nonconformist. He was always ahead of time and, therefore, usually out of phase with his contemporaries. By the time his ideas became accepted he had already forged ahead to take up a new attitude. Szilard himself illustrated this characteristic in a story which he liked to tell about himself. He served once on a jury in a murder case. When the first vote was taken, eleven jurors were in favour of convicting, but one— Szilard—was for acquittal. Since unanimity was required, the discussion was resumed and Szilard expounded his arguments. After some time another vote was taken; the result was again eleven to one, but this time eleven were for acquittal, and one for conviction: the odd vote was Szilard's who had in the meantime changed his mind!

This nonconformity is partially responsible for the fact that for a man of his tremendous achievements and influence, he had remarkably few publications; he published less than thirty papers in scientific journals. However,

he had written a number of reports for the Manhattan Project (war-time work on the atom bomb), articles, memoranda and letters which contain many original ideas, both scientifically and sociologically; much of this material is of immeasurable value to the historian of science and current affairs. It was, therefore, an admirable and public spirited act by Professor B. T. Feld (who collaborated with Szilard in science and in world affairs) and Dr Gertrud Weiss Szilard (Leo's wife) to undertake the task of collecting and editing all his work. The first volume which has been published so far contains Szilard's scientific contributions. Apart from reprints of papers which appeared in various journals, it contains in full the reports relating to the Manhattan Project and much other material published for the first time.

It was an ingenious idea of the editors to divide the volume into several sections, each dealing with a specific area (thermodynamics, nuclear physics, Manhattan Project, biology, patents) and to precede each section with an introduction by a person who collaborated with Szilard in that particular area. These introductions, together with the foreword by Jacques Monod, the preface by the editors, and the *curriculum vitae* written by Szilard himself, make it much easier for the reader to understand Szilard's personality and to evaluate the importance of his contributions. The proper juxtaposition of published papers with private letters and declassified reports helps to fill in gaps, and to emphasize the role played by Szilard in one of the most notable periods in science.

Szilard was primarily a theoretician but his engineering upbringing enabled him to devise experiments which always worked. He had an uncanny instinct for the essential elements in a given field, be it nuclear physics, technology, biology or politics, and concentrated his efforts on those. Although he never headed a department of his own, he always managed to induce people to collaborate with him. For most of his

life he was a knight errant, wandering from laboratory to laboratory, and leaving his mark in each place of halt. In 1934 he paid a short visit to St Bartholomew's Hospital in London, and in the course of a few months made several important discoveries, including the Szilard–Chalmers reaction, which put the Physics Department at Bart's, perhaps the smallest at that time, on the world map of nuclear physics.

His most important role was probably in relation to the release of nuclear energy. His own account makes fascinating reading. In 1933, soon after the discovery of the neutron, Rutherford was reported to have said at a meeting of the British Association that talk of large scale liberation of atomic energy was moonshine. This piqued Szilard, who felt that neutrons, which do not ionize and, therefore, must interact with nuclei, could be used to produce a chain reaction in which the capture of one neutron would give rise to the emission of further neutrons. Not knowing which nucleus would be most suitable, he wanted to carry out a systematic survey of all ninety-two elements; the cost of this project was estimated to be $8,000. However, the funds did not materialize and the survey did not get under way. It was not until 1939, after the discovery of fission, that he observed —at the same time as Joliot—the emission of neutrons, thus opening the way to a practical chain reaction. He followed this up very quickly with the design of a nuclear reactor for which he filed and was later granted a patent.

Speculating what would have happened if fission of uranium were discovered—as it should have been in 1934, and considering the political situation in Germany at that time, Szilard concluded that those who missed this discovery should have been awarded the Nobel Prize for Peace! Somehow, the Nobel Prize—whether for Physics or for Peace—eluded Szilard, but posthumously he achieved another unique distinction: a crater was named after him on the far side of the Moon, an appropriate memento to the man

who dared to defy Rutherford in showing that nuclear energy was not "moonshine". Actually, the naming of a crater after him was predicted by Szilard in his book, *The Voice of the Dolphins,* in connexion with his political activities, but this is another story, which will be told in the second volume of the *Collected Works of Leo Szilard.* Its publication is eagerly awaited.

J. ROTBLAT

Neurotransmission

Perspectives in Neuropharmacology. Edited by Solomon H. Snyder. (A Tribute to Julius Axelrod.) Pp. xi+404. (Oxford University: London and New York, September 1972.) £7.75.

THIS book contains twelve articles written by former colleagues of Dr Julius Axelrod, to whom the book is dedicated. The articles give a picture of the main direction of research into chemical transmission in the brain, and into the biochemical processes involved in transmitter metabolism. The articles form an interesting and valuable collection.

L. T. Potter and P. B. Molinoff describe the isolation of cholinergic receptor proteins. A receptor antagonist resembling a choline ester (benzilylcholine mustard) has been synthesized by Gill and Rang. This is an irreversible blocking agent of muscarinic receptors. Potter and Molinoff find that alpha-bungarotoxin, obtained from the venom of a snake common in Taiwan, is a specific labelling agent for nicotinic receptors. The toxin blocks all responses to acetylcholine (ACh) in electric tissues (of *Torpedo*) and skeletal muscles, without affecting resting or action potentials, the release of ACh, or acetylcholinesterase. A comment may be made on the authors' use of the term "cholinergic". Dale used the term to distinguish sympathetic fibres which "worked" through the release of ACh (like those to the sweat glands) from those which "worked" through the release of something like adrenaline; these were adrenergic. Hence "cholinergic" can be applied to nerves, but not to receptor proteins.

S. H. Snyder and K. M. Taylor deal with histamine in the brain, and discuss whether it is a transmitter. Histamine is synthesized maximally in the hypothalamus. It appears to be localized to nerve terminals in the adult rat brain and to be contained in synaptic vesicles. But histamine is peculiar in occurring in higher concentration in the newborn rat brain than in the adult. There is no evidence that there is an uptake of histamine by nerve terminals as there is of noradrenaline.

L. L. Iversen has written on the uptake, storage, release and metabolism of GABA in inhibitory nerves. This article is full of interest. Gamma-aminobutyric acid is now known to be released by the inhibitory neuromuscular nerves of crustaceans, and also by the inhibitory fibres from the Purkinje cells of the mammalian cerebellum which run to Deiter's nucleus. The inhibitory action is due to the transmitter stabilizing the resting membrane potential of the postsynaptic cell, and GABA does this by causing a selective increase in the permeability to chloride ions, thus stabilizing the membrane near the chloride equilibrium potential. A second way in which the inhibitory transmitter may act is at synapses on presynaptic excitatory terminals to reduce the amount of excitatory transmitter released. GABA mimics very closely the action of the naturally occurring inhibitory transmitter; it is present in high concentrations in inhibitory motor neurones, but not in excitatory neurones. The enzyme which synthesizes GABA (glutamate decarboxylase) is present in inhibitory neurones, but not in motor neurones. The alkaloid bicuculline blocks the actions in the mammalian brain, and also the naturally occurring inhibitory transmitter at neurones (insensitive to strychnine) in the cerebral cortex, the cerebellum and the hippocampus. GABA-inhibitory neurones have a specific GABA-uptake mechanism, and mammalian brain slices accumulate exogenous GABA. Release of GABA by the stimulation of the inhibitory motor nerve has been demonstrated in the lobster nerve-muscle preparation. The amount released is proportional to the frequency of stimulation.

R. J. Wurtman and J. D. Fernstrom write on the control of brain monoamine synthesis. They have found that physiological changes in plasma tryptophan influence the amount of serotonin in the brain. Thus administration of a low dose of 12.5 mg kg⁻¹ tryptophan to rats at a time when plasma and brain concentrations are lowest causes an increase in brain serotonin of 20–25%. The administration of doses of insulin (1–2 U kg⁻¹) which cause a rise in plasma tryptophan also cause a rise in brain tryptophan and serotonin. A carbohydrate meal eaten by a rat also causes a rise in plasma tryptophan, brain tryptophan and brain serotonin. This may be due to the secretion of insulin caused by the meal.

H. Thoenen writes on chemical sympathectomy by 6-hydroxydopamine, an amine which is taken up by adrenergic neurones and in large doses causes degeneration of the terminals. In the newborn animal it causes degeneration of the ganglion cell bodies. In the adult cat nictitating membrane this degeneration lasts for about 14 weeks. When a large dose is given to a cat, and the heart is then perfused, there is a long lasting discharge of noradrenaline. This discharge does not occur in the absence of calcium. Evidence that 6-hydroxydopamine must first be taken up is provided by the fact that its action is blocked by desmethylimipramine which prevents the uptake of noradrenaline. Thoenen says that the changes produced by 6-hydroxydopamine do not affect the Schwann cells or cholinergic nerve endings. However, he does not say whether the narrow band of acetylcholinesterase, which Eränkö showed closely investing the adrenergic terminals in the rat pineal, is affected.

J. H. BURN

Logic Design Techniques

Logical Design of Digital Circuits. By C. M. Reeves. Pp. v+192. (Cambridge University: London, November 1972.) £1.60.

Logic Design Algorithms. By D. Zissos. Pp. x+458. (Oxford University: London, November 1972.) £9.

THERE are already so many books published on logic design techniques that the appearance of yet more texts must be viewed with some apprehension; however, these new books appear to offer a somewhat different approach to the subject.

Logical Design of Digital Circuits is intended primarily for computer science students and, as such, adopts a formal mathematical approach to the subject, drawing heavily on Boolean algebra. In many cases this over-complicates the subject, especially for engineers, and a more physical interpretation would have been preferable. For example, the solution of simultaneous Boolean equations is excellently dealt with and is given a fairly detailed treatment. However, though in theory simultaneous equations are important, particularly in the design of sequential circuits, in practice they are seldom, if ever, used.

It is very encouraging in this book to see software techniques being considered as an integral and alternative aspect of logical circuit design; the two disciplines have been separated for far too long. Further progress in the design of logic systems depends very much on the realization and acceptance of the duality of hardware and software implementation. In particular the use of Backus–Naur Form for defining binary sequences, as for example in describing the operation of finite-state machines, is to be applauded. It is interesting to note in this respect the similarity of BNF to the regular expression method of defining sequential machines. Another useful feature of the book is the emphasis on logic simulation, and the inclusion of an ALGOL listing for a simple simulator package called SOLD.

Overall the book is fairly comprehensive, including chapters on Boolean algebra, the design of combinational circuits, and clocked sequential networks, and concludes with a chapter on computer circuits; the subject of asynchronous logic is omitted entirely. There are very few errors in the book, but there are a number of misleading assumptions: for example, relating the cost of a circuit directly to the number of inputs. In addition the logic symbols used could have been better specified; for instance, bistables are shown without a clock input: this can be misleading, as in the case of the circuit of Fig. 2-11, which would malfunction unless the bistable was clocked. The book contains numerous problems, some of which have worked solutions; a short bibliography is given at the end of the text. In my view the book is good value and could certainly be recommended (with some provisos) as an introductory text for computer science students.

Logic Design Algorithms is primarily intended to be a handbook of design techniques for the professional engineer, and as such it adequately fulfils its function. The text gives detailed algorithms (fourteen all told) for the design of combinational, asynchronous and synchronous logic, using NOR/NAND gates and bistables for the implementation. The book, however, has a rather curious approach to the subject and gives the impression that the work, though highly original, has been developed independently of established switching theory. This has the disadvantage that it would be difficult for the non-specialist to relate the terminology used in the text to existing work. For example, in the discussion of asynchronous logic no mention is made of the usual circuit classification into fundamental mode, normal mode, pulse mode, and so on.

The algorithms themselves, based as they are on algebraic techniques, seem rather too complex for hand computation. It is intended, however, that the algorithms should eventually be implemented on a digital computer for automatic computation. The design methods used achieve good results, particularly in the case of combinational circuits which allow non-canonical input terms and take account of hazard-free and multi-level implementation. Unfortunately, there are a number of important points which require further clarification. For example, in the discussion of circuit hazards no mention is made of dynamic hazards due to unequal signal paths; it would appear that the algorithms do not allow for this condition.

The techniques described for sequential circuit design do not seem to offer any great advantages over existing methods. The derivation of turn-on and turn-off sets, and their subsequent

reduction, is directly analogous to the usual practice of extracting bistable input equations. Moreover, the algorithms can be at fault when dealing with don't-care conditions. For instance, in Fig. 4.46b B and $\overline{B}$ both go to logic I for the input condition $\overline{A}$ B K C, indicating that the SR bistable input constraint of SR=0 has been violated.

The book contains a copious number of worked examples in the text and an appendix of specimen test papers; very little reference is made to current work in the field, and there is no bibliography. Though it is suggested that the book would be suitable for student use, in my opinion this is not so, due to the unusual treatment of the subject.

D. W. LEWIN

Propaganda and Eugenics

Genetics and American Society. By K. M. Ludmerer. Pp. xi+222. (The Johns Hopkins Press: Baltimore, Maryland, 1972.) $10.

THOSE historians and theorists intent on dismissing the "use–abuse" model of the interaction of science with society would do well to read this book carefully. They may be hard pressed to suggest an alternative explanation of the events described. Though "genetic science is intimately related to society", Mr Ludmerer has unravelled enough threads in the past fabric of that science to show that its relations are not necessarily ideological; that most genetic research is and has been intellectually independent of the old-style eugenic social activism which "abused" its findings.

Eugenists and their supporters, from the early years of this century until the 1930s, claimed a scientific base for their often prejudiced political and social goals. Most human geneticists saw very early that their theories were being misused and ceased to support eugenic proposals. That the eugenists were, in America, successful in putting through state sterilization laws and the Federal Immigration Restriction Act of 1924 was a function of their political strength rather than their scientific support. Geneticists of the time despised eugenics, but did not have effective institutional bases from which to oppose eugenic propaganda. Indeed, eugenic abuses had a devastating effect on the advance (measured in terms of public support, financial endowment, publishing outlets, and so on) of genetic science itself. After the Second World War, however, longevity and the atomic bomb brought new ("clean") medical and scientific interest in human population and radiation genetics. At the same time, American revulsion at Nazi eugenic actions killed the old move-

ment, and left new, rather less strident and more theoretical, eugenics groups. The present-day eugenics picture contrasts strongly with the racialist, authoritarian and simple-minded view of interwar eugenists; and human genetics has, of course, become thoroughly respectable.

This is the story Mr Ludmerer tells, in a fairly well-written fashion, although he is a little repetitive and fond of quotations. His published and archival documentation is thoroughly scholarly, and primary material is usually interpreted with care. But Mr Ludmerer's recent interviews with the scientist-actors of his story constitute secondary sources, which he too often takes at face value. This is understandable in view of the libel laws, but it does lead to some white-washing of the "everybody-else-was-a-racist-but-not-me" variety.

Finally, there are three small interpretive "mistakes" in the book: (1) Mr Ludmerer underrates the quality of membership in the early British Eugenics Education Society, and the influence of British eugenists generally; (2) he has an unhealthy negative attitude towards amateur scientific activity; (3) he does not recognize the very complicated way in which "biologism" in sociology retained and expanded its influence, while seemingly losing it.

But these minor faults do not affect the importance of the book as perhaps the best history to date of the social aspects of American genetics and eugenics. It is a valuable contribution to our understanding of a subject about which we must remain politically, socially and intellectually sensitive.

JAMES FRIDAY

Mechanical Design

The Selection of Design. By Gordon L. Glegg. Pp. 84. (Cambridge University: London, November 1972.) £1.85; $6.95.

IN a first approach to design there is a tendency to divide it into three areas: visual design, mechanical or structural design, and the rest. It is in this sequence that design is appreciated popularly and, as we may note, by politicians. At the national level the official stimulation of design has now passed from the Council of Industrial Design (visual mode) to its transformation the Design Council (visual plus mechanical mode).

Interesting and valuable aspects of design such as involve electronic circuits, computer software, chemical processes, and so on, lie within the *terra incognita* of the third area. Ongoing arguments suggest that architects are uncertain about the areas to which they owe allegiance.

After this preamble it is possible to

state that Glegg's book uses "design" in the sense of the second area. This is implicitly the only place where design takes place. It is a rather boring place where "there is no unsophisticated engineering left, or there shouldn't be". What this means is that most of the basic devices or ways of doing things have already been invented or discovered. From this notion derives the term "selection" in the title of the book. The activity of design is largely concerned with the selection of possible ways of doing things from an apparently existing catalogue. From the many possibilities one eliminates by selection by context and by selection of content. Somehow economics takes a back seat. Very occasionally there are apparent impossibilities to tackle. This is the creative activity.

Within his limits Glegg has produced a very interesting little book which is essentially of the "how I" rather than the "how to" kind. Whether it will be suitable to young inventors will depend upon their lines of activity. In some ways they may have to be interested in the bits and pieces of motor cars. But there is no suggestion of further reading or hints of what other people have been doing in the design business and how his ideas compare with theirs.

SYDNEY GREGORY

Photosynthetic Enzymes

Methods in Enzymology, Photosynthesis and Nitrogen Fixation. Edited by Anthony San Pietro. Volume 24, Part B. Pp. vii + 526. (Academic: London and New York, September 1972.) $23.50.

AN up-to-date method book for photosynthesis research has been needed for a long time. The present book fills this need by giving an almost full account of a vast number of experimental approaches, ranging from biochemical to physical, to this multi-faceted subject.

Of the two volumes dealing with photosynthesis and nitrogen fixation, part A has been devoted to preparatory methods. Part B, which is the matter of this review, is less homogenous; its main body is devoted to processes and measurements, but it includes preparative aspects as well in the sections on "Synthesizing Capabilities" and "Nitrogen Fixation".

The book is divided into four sections, containing forty-four chapters, each dealing with a different methodological aspect and written by a different author. Although this guarantees, in general, authority and a high standard of presentation, the book as a whole suffers from a lack of homogeneity and coherence. This could be

perhaps eliminated by elaborate editing and planning. The various chapters should have been grouped together according to being physical, chemical or biochemical, and further subgrouped into various sub-categories. For example, optical and photophysical methods could be grouped together, with an appropriate unifying introduction. The same is true with other categories. The division to small chapters also causes unnecessary repetition. For example, light intensity measurements are included in the chapters "Quantum Yields" and "Light Intensity Measurements". There are other examples of this.

The level and depth of the presentation are not equal. Besides very comprehensive treatises (to mention but a few: "Flash Kinetic Spectrophotometry", "Light Induced Paramagnetism", "Measurement of Hill Reaction") there are some small chapters that miss essential details. For example, methods of treating data in order to obtain the limiting quantum yield are absent; the chapter "Enhancement", besides defining the subject, gives just little more than how to measure a Hill reaction, and particular aspects regarding how to treat the data and methods to deal with non-linearity of rate with intensity (for example, the Kok effect) are not expanded; the small note on "A Green Safelight" could be expanded and included in the chapter on "Light Sources and Measurements"; the coverage of fluorescence and delayed light methods is too brief; the details of measuring O_2 evolution from single flashes, and the detection of other redox reaction by the oxygen electrode, although mentioned, are also too brief.

There are descriptions of very specific methods, which have not been extensively and independently reviewed. For example, the method of high derivative absorption spectrum to separate peaks in a complicated spectrum should be applied with caution (since each derivative adds, in principle, an additional peak to the original spectrum) and probably is valid only under limited conditions. Also, the method of steady-state relaxation spectrophotometry, although a very general tool in chemical kinetics, seems to have only a limited application here.

The coverage of the typical biochemical and preparative chapters seems adequate. In fact, the writing of a typical biochemical method involves far fewer problems and is more or less standardized compared to the writing of a physical method.

These drawbacks, serious as they are, do not impair the usefulness of the book, which serves as a quick reference and source for most of the methods existing in the field, and is thus very welcome. S. MALKIN

Extinction by Hormone

Insect Juvenile Hormones: Chemistry and Action. Edited by Julius J. Menn and Morton Beroza. (Proceedings of a Symposium held in Washington, September 1971.) Pp. xv + 341. (Academic: New York and London, June 1972.) n.p.

Insect Sex Pheromones. By Martin Jacobson. Pp. xii + 382. (Academic: New York and London, October 1972.) $22.50.

JUVENILE hormone functions during insect metamorphosis by actively favouring the differentiation of larval characters, and in many species it also controls oocyte vitellogenesis in the adult female. If the corpora allata—the glands which produce juvenile hormone—are removed from early larval instars, dwarf adults can result, and if the hormone is introduced when it is normally absent, supernumerary larval instars or monsters intermediate between larva, pupa and adult can be produced. Moreover, when juvenile hormone is applied to the eggs of some insects, embryogenesis can be abnormal or post-embryonic development can be affected. It is not surprising, therefore, that the prediction was made that juvenile hormone could prove to be a potent insecticide—with the advantages over current synthetic insecticides that, being a natural compound, it would be unlikely to have adverse environmental effects, and that the insects would be unlikely to develop immunity to one of their own hormones.

Juvenile hormone was discovered nearly forty years ago, and its chemical identity was established in 1967 as methyl 10,11-epoxy-7-ethyl-3,11-dimethyl-2-6-tridecadienoate. A second hormone, with a methyl group replacing the ethyl at C_7, was described a short time later. In the years immediately before the identification of juvenile hormone, other chemicals were discovered which mimicked its activities, and families of compounds are now known which have greater or less juvenile hormone activity in a variety of insect species. These discoveries raised the possibility that hormonomimetic chemicals could be tailored for use against specific insect pests.

Insect Juvenile Hormones discusses these aspects of juvenile hormone and its mimics in the light of recent evidence. The volume contains contributions on the chemistry, biochemistry, metabolism and action of the authentic hormones, and of many hormonomimetic chemicals. Preliminary field trials of some of the compounds are described, together with tests on their environmental stability and decomposition products. Very brief details of their toxicity to mammals and plants are also provided.

The papers are reproduced by a photographic process to hasten publication and the consequent differences in style and format are sometimes disconcerting, especially when the text appears to run on into the legends of tables and figures.

Overall, the impression gained from this volume is one of muted optimism. Professor Schneiderman points out that young larvae seem to be quite insensitive to the compounds, which is unfortunate since these stages often cause most damage. Moreover, insects can inactivate, sequester or excrete juvenile hormone at certain stages in their development, so the hope of not developing immunity to exogenous hormone is unlikely to be fulfilled, even more so with foreign chemicals. The results of the field trials are disappointing, although some compounds show promise in the control of certain insect pests. The hormones and their mimics operate during critically short developmental periods, so that application must be precisely timed or the compounds must persist for adequate periods. Results described here suggest that field stability is low. The compounds do not have the dramatic knockdown properties of current insecticides and the effects of application may not be manifest until the next generation. Their use as ovicides seems the most encouraging, for they can be applied to the adult female or her freshly laid eggs, and if embryogenesis is not interrupted, metamorphosis may subsequently be prevented. Considerably more needs to be known of the detailed developmental life-histories of insect pests and the ways in which juvenile hormone and its mimics control and affect morphogenesis, reproduction and behaviour before the hope of specifically tailored insect pesticides becomes a reality. But these "third generation insecticides" will undoubtedly play a major part in any programme of integrated control of insect pests.

Insect Sex Pheromones also contains a chapter on natural chemicals in insect pest control: sex attractants can be used to lure members of the opposite sex in large numbers to particular sites. Or the atmosphere can be saturated with the attractant, causing confusion and disruption of the normal orientation mechanisms so that mating is prevented. This form of control suffers from one of the disadvantages of the juvenile hormone mimics—that the damaging young stages are unaffected and the agriculturalist must look beyond the loss of his current infected crop to subsequent pest-free growth. The author has collected an enormous amount of factual information on the occurrence, identification and synthesis of insect sex attractants, but presents it in this volume in a catalogue style with

little attempt at synthesis or the development of concepts and theories. With 1,337 publications listed, the book will be invaluable as a reference source.

Both *Insect Juvenile Hormones* and *Insect Sex Pheromones* illustrate the results of fruitful marriages between chemistry and biology, which should engage the hopeful interest of all those concerned with the environmental problems of current insecticide pollution.

K. C. HIGHNAM

Carbohydrates

Stereochemistry of Carbohydrates. By J. F. Stoddart. Pp. xi + 249. (Wiley Interscience: New York and London, 1971.)

ONLY infrequently is a new textbook sufficiently unusual to have no near competitor. Dr J. F. Stoddart has written such a book and in doing so has presented carbohydrate chemistry in a new light, and moreover in a way designed to attract the attention generally of organic chemists. In the past there has been a tendency to treat carbohydrate chemistry as an isolated aspect of organic chemistry, rather than as part of aliphatic and heterocyclic chemistry. However, many of the problems which arise in carbohydrate chemistry are stereochemical in nature and answers are to be found in a knowledge of the structural and dynamic aspects of stereochemistry. In this book there is a thorough but concise account of carbohydrate chemistry in stereochemical language. The important role of isomerism in carbohydrate chemistry is high-lighted and the account serves to illustrate the almost unique status amongst organic compounds of the sugars, because constitutional, configurational and conformational isomerisms are often superimposed on each other in this group of natural products. The author has achieved a happy union of stereochemistry and carbohydrate chemistry.

The book has five chapters, each concluded by a list of references, and an author and subject index. In the first two chapters basic principles are presented and so to use the book little previous knowledge of modern stereochemical concepts is required. Definitions are clearly stated. Other chapters are devoted to the constitutional, configurational and conformational isomerism of sugars; the interplay of these forms is explored. To avoid confusion arising from the specialized and often bewildering nomenclature of carbohydrates, many illustrations are provided, to the extent that a formula is given for almost every compound mentioned. Discussion of the stereochemistry of polysaccharides has been inte-

grated with that of simpler carbohydrate derivatives.

The physical methods which are particularly suited to providing answers to stereochemical problems posed by carbohydrate molecules are surveyed. These include X-ray diffraction, mass spectrometry, infrared and nuclear magnetic resonance spectroscopy, dipole moments and optical rotations. This coverage is commendable because in the investigation of stereochemical problems it is desirable to employ as many physical techniques as possible.

The book is excellent for its description of the systematic application of conformational principles. It is surprising, and even unfortunate, that those concerned with conformational analysis have not drawn extensively on carbohydrates to exemplify conformational principles. It is not always appreciated that carbohydrate chemistry has made important contributions to conformational theory. For example, the term "conformation" was first introduced by Haworth in 1929 in connexion with the shapes of sugar molecules, and cellulose is probably the first molecule in which the chair shape of the six-membered ring was detected through X-ray analysis. The effect of conformation on reaction rate was probably first recognized in carbohydrates by Isbell in 1937, and Reeves's discussion in 1949 of the conformations of sugars antedates by a year Barton's pioneering paper on conformational analysis. The first major recognition of the importance of conformation in n.m.r. spectroscopy is found in a paper in 1958 by Lemieux, Bernstein and co-workers. The author's readable account of the facts (both qualitative and quantitative) of carbohydrate conformations, and his discussion of concepts, should stimulate investigators in other branches of organic chemistry to turn to carbohydrates as suitable, and often readily available, models to illustrate or confirm stereochemical principles.

The book will be of interest also to graduate students and research workers in organic stereochemistry and natural product chemistry, as well as to those specializing in carbohydrate chemistry and conformational analysis. Teachers of degree courses in chemistry will find valuable reference material. Extensive use of the book over a period of months has shown it to be both reliable and informative. The selection of topics for discussion in the book is necessarily personal to the author, but is sufficiently wide to achieve adequately the aim of bridging the gap between carbohydrate chemistry and stereochemistry. This is a textbook which was badly needed. The author is to be congratulated on his efforts and his book is strongly recommended.

W. G. OVEREND

Nature's Allograft

Nature's Transplant. The Transplantation Immunology of Viviparity. By J. Maxwell Anderson. Pp. viii + 145. (Butterworth: London, November 1972.) £3.

A MAJOR unsolved problem in transplantation biology is how the mammalian embryo manages to survive in the uterine environment of a genetically differing female without eliciting the expected immunological rejection reactions. The embryo seems to be exempt from the "laws of transplantation immunity", and as such is of considerable interest not only for its own sake but for the possibility of providing valuable clues to the attainment of successful surgical grafts of tissues and organs and to an understanding of the cancer–host relationship.

The precise nature of the problem was defined in 1953 in an eloquent essay by Medawar[1], and most of the experiments subsequently carried out in attempts to elucidate this paradox of transplantation immunology have been within the philosophical framework of that assay. Maxwell Anderson's short book is essentially a contemporary assessment of the old problem. It deals comprehensively with various theories put forward by Medawar and others, and considers much evidence to support or undermine them. The embryo's survival is undoubtedly due to a number of biological adaptations, including the specialized nature of its vascularization, the selective placental "barrier" restricting any large-scale traffic of maternal immunologically competent cells, and the establishment of a complex foeto-maternal immunological equilibrium following exchange of antigenic information. The presence of blocking antibody is thought to be one of the factors involved in this equilibrium.

Despite the blurb's assertion that "This is the first unified account of the subject", Anderson's analysis is very much in line with many of the reviews that have appeared in the past four years, although his "Integrative Hypothesis" of chapter 7 does include one or two new thoughts. The book contains eight plates on embryology and tissue grafting in the armadillo, which might be thought excessive considering the wide scope of the text.

In general, it is difficult to see the market for this book. It is far too detailed for anyone not involved in research in the field (no fewer than seventy pages out of the total of 145 are taken up by reference lists), whilst those that are would probably find Beer and Billingham's recent review[2] of more value. W. D. BILLINGTON

[1] Medawar, P. B., *Symp. Soc. Exp. Biol.*, **7**, 320 (1953).
[2] Beer, A. E., and Billingham, R. E., *Adv. Immunol.*, **14**, 1 (1971).

Solid State Spectroscopy

Optical Properties of Solids. By Frederick Wooten. Pp. xiii + 260. (Academic: New York and London, October 1972.) $12.95.

SPECTROSCOPIC studies provide a wealth of information about the various excitations which occur in crystals, and in spite of the very large amount of research which has already been carried out, solid-state spectroscopy still throws up a steady flow of new phenomena. The book under review aims to supply a distillation of this active research field, with the fundamental principles of the subject described at a level suitable for first-year graduate students. The material is restricted to the optical properties associated with electronic transitions in perfect crystals. There is some discussion of surface effects in addition to the more familiar bulk properties of electronic excitations in the effectively-infinite crystal. The author is concerned throughout the book to explain the theoretical concepts behind the spectroscopic properties. He has taken pains to provide simple derivations of the main theoretical expressions, and it seems to me that his mixture of mathematical rigour and physical insight achieves a suitable balance for his intended readers. The theoretical results are illustrated throughout the book by a well-chosen selection of experimental data, but the emphasis of the work is theoretical, and there is no attempt to provide a survey of experimental results or techniques.

The main topic of the book is the interaction of electromagnetic radiation with electronic transitions. The quantum mechanics of transition rates, absorption and dispersion of radiation is presented in some detail. The dielectric function is used throughout as a bridge between the microscopic electronic properties of solids and the macroscopic concepts used in the description of optical phenomena. The associated theoretical machinery of linear response functions and the fluctuation-dissipation theorem is covered, with particular reference to electronic spectroscopy. Typical spectra of metals, alloys and semiconductors are described and interpreted in terms of the theory. The techniques of photoemission and characteristic energy-loss spectroscopy are shown to be valuable for the complementary information they can provide on the electronic energy-band structure.

The book can be recommended to readers with a good basic knowledge of solid-state physics and quantum mechanics who need a more specialized introduction to electronic spectroscopy. The style of writing and the printing are very readable, and the book is well produced except for a number of misprints which include the complete omission of equation (3.75) from the review copy.

RODNEY LOUDON

Multivariate Statistics

Multivariate Statistical Analysis: a Bibliography. By T. W. Anderson, Somesh Das Gupta and George P. H. Styan. Pp. x + 642. (Oliver and Boyd: Edinburgh, 1972.) £10.

THIS new bibliography is one of those immeasurably important pieces of professional housekeeping to which no review can ever do full justice. Recalling that the senior author, Anderson, is the doyen of statisticians in this field of analysis, it is interesting to note that the project started (in 1963) from the desire of the three authors to understand and increase their own knowledge of the subject. This leads to a systematic search of the literature and on to a massive cooperative organization involving a computer-produced listing and large-scale photography of typescript.

The first chapter covers the available books, a classified list of 213 titles together with an author index, available in 1970 or earlier. This is followed by a chapter on the structure of the 819 journals and other collections of papers used, and here the terminal date is 1966, although there are some items in the Addenda at the end of the volume. The third chapter contains the core bibliography of the (nearly) 6,100 papers arranged alphabetically by author with analysis by year, language, numbers of authors and papers. This, of course, is the computer-produced portion and is a fine example of its kind; the organization is of general bibliographic interest. The collection of papers is indexed in chapter 4 in accordance with a subject-matter code described in detail in chapter 5 where is also found a straightforward index to this subject-matter code.

The preface contains a clear statement of the conditions for complete or selective coverage of the various aspects of this immense field of statistical techniques. At once it illustrates how real boundaries are growing less distinct as well as the need to draw some boundaries or be selective if any usable work is to result.

The statistical profession's collection of works of this kind is steadily improving and the authors, together with everyone associated with ABOMSA (as it has been affectionately styled), merit warmest congratulations and thanks for their magnificent contribution. W. R. BUCKLAND

CORRESPONDENCE

Keynesian or Galbraithian?

SIR,—Surely government spending on research is wise economic policy, not because it is Keynesian, as you suggest (*Nature*, **240**, 515 ; 1972), but because it is Galbraithian. A non-growth economy, such as Galbraith and others have described, will need a place for the able and energetic individuals who in the past have found their rewards as entrepreneurs. Research is as open-ended as business or industry: it can absorb all the enthusiasm of the most able person. But research uses few natural resources, causes little pollution, and seldom contributes in any substantial way to the growth of the economy.

Is it not better for society to pay a man to do research, rather than to pay him to produce and sell goods which society neither wants nor needs? Subsidies to academics and artists to keep their talents out of business and advertising should have at least as high a priority with the government as subsidies to farmers to use their land for one crop rather than another. If we start now to increase the number of research studentships, as well as the funds for research itself, able undergraduates and schoolchildren will tend to steer towards a career in research rather than in business, and there will be fewer frustrated managers in 20 years time.

A substantial increase in the number of people who are focusing a trained curiosity on all aspects of mankind and his world could lead to a new burst of understanding, of the kind last seen during the Renaissance. We can have no more noble aspiration than to try to discover who we are and where we are going. Academics should point out to governments not just that research can be useful in the short term, but also that non-utilitarian research can be valuable.

Yours faithfully,
D. A. MARVIN
298 *Lawrence Street,*
New Haven, Connecticut 06511

Taxonomy and Evolution

SIR,—Professor J. W. Fairbairn queries the significance of the idea of evolution in the advancement of taxonomy (*Nature*, **241**, 225 ; 1973). He makes very generalized accusations against taxonomists without producing any definite evidence.

I have spent the greater part of the past thirty years in intensive taxonomic study of some tropical families of plants on which previously recorded observations were defective, and taxonomic treatments correspondingly unsatisfactory. I assert that the idea of evolution has always been an essential element in my thoughts on the problems presented by these families. The evidence that organisms have reached their present condition through processes of evolution does not depend only on the taxonomic study of existing organisms ; there is much other independent evidence. Evolution implies that there is a built-in natural classification for organisms ; our problem is to find it. To regard the results of a taxonomic study as potential evidence of the history of evolution in a particular case is not arguing in a circle. Thought on the possible significance of such evidence often leads one to further observations which may throw further light on the subject. The problem is a dynamic one ; to deny phylogenetic thinking is to ignore biological reality. I have attempted to express my ideas on this subject, with reference to some particular families of plants, in a paper entitled "Comparative Morphology, Taxonomy and Evolution" (*Phytomorphology*, **17**, 36 ; 1967) and refer interested readers to that statement.

Yours faithfully,
R. E. HOLTTUM
Royal Botanic Gardens,
Kew

Noah's Ark

SIR,—We were pleased to see that your correspondents, Harkins, Stenzel and Black (*Nature*, **241**, 226 ; 1973) have noticed that our paper on protein polymorphisms in man (Haigh and Maynard Smith, *Genet. Res.*, **19**, 73 ; 1972) lends some support to the biblical story of Noah's Ark. What your correspondents have not appreciated is that the biblical story provides the best direct test of Kimura's neutral mutation theory at present available. There are as usual some internal inconsistencies in the account, but it is reported in Genesis, 7, 2–3, that only one pair each of the unclean animals were admitted to the ark and seven pairs each of the clean animals. It follows that if Kimura is right there should be a greater degree of polymorphism in cows and antelopes than in pigs, camels and ossifrages.

Yours faithfully,
JOHN HAIGH
JOHN MAYNARD SMITH
Mathematics Division and School of
Biological Sciences,
University of Sussex

Darwin and the Creator

SIR,—Surely it is silly of J. W. Fairbairn (*Nature*, **241**, 225 ; 1973) to "treat the Genesis account of creation with as much respect as that of the biologist". The fact that the biological accounts are varied and unsubstantiated does not in itself mean that any other account has therefore to be put on the same level. Hypotheses come not only as rivals but in rival forms: the various biological accounts of creation fall into one form, whereas religious accounts fall into another form. Quite apart from the more detailed questions of scientific modelling, how does the Book of Genesis stand in regard to the principle of falsification?

The words by Darwin, which J. W. Fairbairn quotes, include in themselves this contrast, for the concept of a Creator is utterly different from that of the "fixed law of gravity". If one assumes the former, why should one accept the latter, and *vice versa*? The two concepts spring from models of the universe which are incompatible.

It is as well to remember that when Darwin published the *Origin of Species* he did so with an anguished regard to the nature of the society in which he lived and worked. He himself was a firm agnostic and his use of the word Creator must be taken as poetical in the same way that any sensible person takes the Book of Genesis itself.

Yours faithfully,
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Obituary

Lord Rosenheim

LORD ROSENHEIM, KBE, MD, FRCP, FRS, Emeritus Professor of Medicine at University College Hospital, London, and President of the Royal College of Physicians from 1966 until March of this year, died on December 2, 1972, at the age of 64. From 1950 to 1971 he was Professor of Medicine at London University and Director of the Medical Unit at University College Hospital Medical School.

He was knighted in 1967 and became a life peer in 1970, being created Baron Rosenheim of Camden. He was appointed Chairman of the Medicines Commission in January 1972 and in May was made a Fellow of the Royal Society by special election.

Max Leonard Rosenheim was born on March 15, 1908, and educated at Shrewsbury School, St John's, Cambridge, and University College Hospital, where he graduated in medicine in 1932, taking the MRCP in 1934 and proceeding MD (winning the Raymond Horton-Smith Prize) in 1938. From 1941 to 1946 he served in the RAMC, first as a medical specialist and then as consulting physician to the Allied Land Forces in South-east Asia. It was this period of his life which gave him his love of travel and his fascination with far-off countries which were to bear fruit again later.

During his undergraduate days at Cambridge he was interested in the mechanism of action of ketogenic diets which were then used for the treatment of urinary tract infections. He soon realized that beta-hydroxybutyric acid was the key metabolite and the related but more stable substance, mandelic acid, was found to be effective in treating these infections. The impact of this discovery would have been much greater had it not been for the nearly simultaneous discovery of the sulphonamides, but mandelic acid is still in clinical use. Rosenheim was also extremely interested in hypertension and was one of the first to convince the medical profession that it really was treatable.

Although these scientific advances were noteworthy, his outstanding contributions to medicine were in the clinical and administrative fields. He had high and humanitarian standards of care for patients as individuals and also a social conscience which found expression in the publication in 1970, with Jessie Garrad, of *Social Aspects of Clinical Medicine* and the setting up of the Faculty of Community Medicine jointly by the three Royal Colleges of Physicians. After the war he became deeply concerned with the various boards of London University, particularly in relation to the medical curriculum and examinations and to the overseas colleges to which London University was in special relationship. As a result he became an expert committee man with his advice being much sought after. The ties abroad were strengthened by his Sims Travelling Professorship (1958) and by his work as adviser for the British Council (of which he was Chairman of the Medical Panel) which took him to Nigeria, Ceylon, the West Indies and India. On these tours he always visited out of the way places and he appeared to know everyone in the overseas universities.

It was during his Presidency of the Royal College of Physicians that he was able to exercise his qualities and his imagination to the full, and the College, in its new Lasdun home, rapidly became one of the foremost centres of postgraduate medical education. Max went everywhere, and while politically we were losing an empire, medically we were gaining one. He persuaded the three Royal Colleges of Physicians to drop multiple diplomatosis and to unite in a common Membership examination —MRCP(UK). The MCQ paper of Part I of this examination became outstandingly successful and applications to take it came in from Ceylon, Egypt, Ghana, Iran, Malaysia and the West Indies. Under him the College appeal was launched, which reached its target of £500,000, and it is still being used for a number of research and other College activities, the best known of which is the campaign on smoking and health. He also started the practice of holding College lectures in provincial centres.

Lord Rosenheim was unmarried, and in spite of his distinguished position he lived an unpretentious life and was held in the greatest affection by all who knew him. He had innumerable friends whom he used to delight with his amusing and stimulating conversation— not only on medical matters but on books, music and fishing, which were his second loves. For many years he lived with his mother, to whom he was very devoted and who died only recently. Although 1972 brought in a new era for him he seemed just as buoyant as ever and ready for new ventures, but it was not to be, and by his death British medicine is the poorer.

How Not to Exploit North Sea Petroleum

THE Public Accounts Committee in the House of Commons has done a public service by making the most thorough examination so far of the way in which the British government has awarded licences to petroleum companies for the exploitation of petroleum and natural gas in the North Sea. The committee's report (*First Report from the Committee of Public Accounts 1972–73*, HMSO, £1.55) has a sorry tale to tell. First, it complains that the government, which might have been forgiven in 1964 for charging too little for exploitation licences at a time when the potential of the North Sea was more or less unknown, has failed to stiffen its terms as it has become clear that the North Sea is a potentially valuable oil field. It is especially disconcerting that the Department of Trade and Industry, now the responsible authority, should have failed to revise its policy after an experiment in tendering for blocks of territory in the North Sea attracted bids totalling £37 million from the petroleum companies. The committee has also drawn attention to the way in which most of the petroleum companies operating in the North Sea may be able to offset their tax bills by subtracting from them taxes already paid elsewhere in the world or losses and development costs incurred in other kinds of operations, running tanker fleets, for example. Although the British government has in the past few years been subjected to some ill-informed criticism on the grounds that it had been too lenient with the petroleum licensees, it is hard to see how it will be able to shrug off the cogent criticisms of the Public Accounts Committee.

The emergence of the North Sea as an important source of energy has been rapid and full of surprises. In the early sixties, it was thought likely that the North Sea would yield substantial amounts of natural gas, for much the same geological reasons as the Netherlands was able to find gas beneath land now dry or close offshore in the early nineteen fifties, but the discovery of substantial oil fields has been a big surprise. From the start, however, the British government has taken the view that the reserves, unknown though they may have been a decade ago, should be exploited as rapidly as possible. This was the starting point for the original decision that the companies licensed to exploit a block of territory should make annual payments which will rise from £10,000 a year in the seventh year of exploitation to a maximum of £72,500 a year as time goes on and that they should pay a royalty of 12½ per cent of the value of the petroleum products extracted. These terms appear to have been influenced by two separate considerations. First, the British government seems to have been anxious not to make life too difficult for the oil companies operating in the Middle East and North Africa by setting terms which might have given the OPEC countries an excuse for increasing their demands. Second, the government was persuaded by its officials that it would in any case recover something like a total of half the value of the oil extracted from the North Sea by taxation of company profits, an assumption that

would have been correct if only the government had understood its own taxation system as well as the oil companies appear to do. The prospect now, however, is that the yield to the British government from the exploitation of the North Sea reserves will be much less than it might have been, and certainly less than other countries such as Norway now have good reason to expect. The gorvernment has only itself to blame if it is now subjected to a chorus of demands from the Labour Party that North Sea gas and oil should be nationalized.

At this stage, it is hard to know what can be done by less drastic policies. The Public Accounts Committee says that the government should consider a revision of the method of taxation on petroleum products, and there would be no inequity in a levy of a fixed amount on each barrel of oil recovered from the North Sea. The government's difficulty, however, is that its agreements with the oil companies do not give it automatic access to operating costs in the North Sea, with the result that it cannot, without the cooperation of the companies, fix a levy that will not be inequitable to the companies and which will nevertheless ensure that the market price of North Sea oil is comparable with the world market price at any time. That is another defect in the present arrangements, which have given the oil companies leases on the most productive parts of the North Sea for a total of 46 years.

On Tuesday this week, the Chancellor of the Exchequer acknowledged that the Public Accounts Committee is right, and agreed that the tax rules should be changed, but there are more general issues to be decided. In the first place, the British government should recognize that the North Sea is not the last of the offshore areas in which oil is likely to be found. Perhaps the Public Accounts Committee is unnecessarily pessimistic in supposing that, now that it has helped to shut the stable door, the horse has already bolted. What is needed is some administrative device for making sure that the selling price of oil and gas should be roughly comparable with the world price for these materials and that it should rise as the world price rises, and yet also allow exploiting companies nevertheless to make a decent profit. There is a certain entrepreneurial simplicity in the device, much favoured in the United States, for putting blocks of land up for auction, and certainly that is a method which does not require that civil servants should understand the economics of the petroleum industry. It has much to commend it. But it would be still better if there were government machinery for fixing the price of oil in the North Sea from time to

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Editor of *Nature*

Formal applications are invited (see page xi of this issue) for the post of Editor of *Nature*, which becomes vacant later this year.

time in tune with the world market price, and if the difference between proven production cost and selling price were shared equitably between the government and the companies. This does not imply nationalization but it does amount to close economic control.

The second general question to which the government should now pay some attention is the untested hypothesis which appears to have guided its exploitation policy for the past decade—the notion that the exploitation of the North Sea should be as rapid as possible. The error implicit in this assumption is that the need to save foreign exchange, and to insulate the British economy from the rising price of OPEC oil, is paramount. The truth is, of course, that no amount of success in the North Sea will make it possible for British needs for liquid fuels to be met exclusively from local sources. Moreover, there would clearly be great hazards in the long-term if the British economy were able to withdraw from the world market and chose to do so. What would happen then when the North Sea reserves are played out, half a century or so from now? How would British industry re-enter the world market? And would it be welcome there? The truth is that the country will remain dependent on a variety of sources of gas and petroleum and that it cannot hope to diminish the economic pressures of the international market by a more rapid exploitation of the offshore reserves. It would be much better, in the circumstances, if the speed of exploitation were determined not by the rate at which physical arrangements can be made for extracting gas and petroleum but by a prudent economic assessment of the most sensible rate of exploitation.

University Computers

THE Computer Board for Universities and Research Councils is a worthy and almost typically British institution. It owes its existence to the recognition, in the 1960s, that universities would not be able to equip themselves with modern computing facilities out of the recurrent grants from the University Grants Committee and that, in any case, structural innovations would be needed if quite small universities were to be given access to quite large machines. The result is that there are now a number of regional centres to which most universities have convenient access, while the growth of computer power has increased substantially. In its latest report, the Computer Board says that in March 1972, the effective machine capacity was ten times that available to the universities in 1965, and the Computer Board now promises that by 1974, the capacity accessible to universities will have doubled again. This is a creditable performance, even if the pace of installation in the past few years has fallen below the estimates of demand prepared at the outset of the Computer Board's existence. And even if it has been necessary to meet some of the demands by throwing the IBM 370 machine at the Rutherford High Energy Laboratory into the common pool, it is also fair to say that this programme has been carried through at comparatively little cost. In the last complete financial year, the Computer Board spent only £9.3 million on its activities.

It remains an important question to know whether the Computer Board should continue indefinitely to exist as a kind of fosterchild of the University Grants Committee and the Science Research Council. At the beginning, the frustration of university researchers seeking access to computer time was a powerful demonstration of the need for university access to large modern computers, and the pattern of regional centres which has grown up is a sensible way of meeting the need. But now that the pattern has been established, and now that there is at least a chance that adequate capacity will be available in the near future, is it not time to consider whether the Computer Board should not be subsumed within either the Science Research Council or the University Grants Committee and preferably the latter?

The advantages of a merger are not clear-cut but they should be considered seriously. First of all, there is now, or may be in the next few years, a tendency to assume that because the Computer Board exists, the universities themselves and the University Grants Committee as a whole should wash their hands of computer policy. The truth is, however, that computers are now as much a part of the essential equipment of a university as were lecture halls and laboratories in the 1940s. It would be in everybody's long-term interest if the provision of computer facilities was regarded as an inescapable charge on the collective budget of the universities. Then the existence of regional computer centres, which have outlived the jealousies which attended their creation, would be a useful organizing principle to include within the British university system. Whether the universities like it or not, financial pressures in the years ahead are certain to force on the University Grants Committee proposals for the grouping and common use of other expensive facilities. It would help the committee, in these battles yet to come, to be able to show that it could run a sensible organization for the sharing of computer time. But the time has also come when universities could play a more vigorous part in specifying the kinds of computer facilities they consider to be necessary. For one thing, the provision of computer facilities for instructional purposes has lagged behind the need, but the universities themselves are the best agents for developing the equipment needed for that purpose.

The question of whose computers should be bought for the universities is a continuing conundrum. The introduction to the Computer Board's report makes it clear that the publication of the 1971 report was abandoned because of differences between the Computer Board and the government on the policy of helping British manufacturers. So far as can be told, these differences have been patched up but not resolved. And in the past two years, the Conservative government has become as attached as its Labour predecessor was to a policy of helping British computer manufacturers to sell their products even in the face of the apathy of potential customers. But is it really sensible that the government should pursue a policy which denies to British universities the best machines for the sake of keeping IBM at bay when the universities themselves are now the most fruitful source of the men and women who will, in the years ahead, be able to help British manufacturers improve their products? The trouble is, of course, that the British government's policy on the computer industry is still inadequately defined. There is very little chance that British computer manufacturers will be able to develop internationally competitive machines in the near future, and there is no reasonable hope that their task will be simplified if they are given an unfair share of the domestic

market in the next few years. What the government has to decide is what kind of computer industry it wants to have ten years from now and how much it is prepared to pay in development costs to achieve that target. It is unthinkable, in present circumstances, that British companies could succeed independently of their competitors in Europe, and even if it did, it would find itself hamstrung by the procurement policy of European governments. The moral is that the British government should abandon its protection of the domestic market and throw its weight, instead, into the building of a European computer industry.

Muddle in America

IT is improbable that the American government, the Administration and Congress lumped together, knows how foolish its budgetary procedures make it seem. After ten months of fierce argument, it now seems to have been accepted in Congress that the battle to force an increased rate of spending on the Administration in health and education has been lost. Our Washington Correspondent reports this week (see page 81) that Congress and the Administration have finally reached a stalemate on the Health, Education and Welfare Bill, as a result of which the level of spending during the current fiscal year (with less than four months to run) will be pegged at what it was last year. Among the scientific organizations seriously affected will be the National Institutes of Health, which have in the past eight months been uplifted first by the Administration's own request for a higher rate of spending and then by Congress's show of still greater generosity and finally have found themselves pegged back to a rate of expenditure essentially the same as that specified in the inadequate budgets for 1971-72. The difficulties that this will cause are easily imagined. Having committed themselves to some of the plans drawn up when it seemed that the budget would be generous, the National Institutes of Health will now find it necessary to cut back on other programmes in principle just as worthy. Moreover, it is programmes in principle just as worthy.

Battles over the budget for the Department of Health, Education and Welfare are, of course, a traditional part of the congressional year. Just as the department itself is accurately known as the antheap, so its annual budget creates a greater variety of controversial issues which may be delayed in Congress itself by arguments over questions such as the bus-ing of negro children to white schools and in the White House if Congress should have committed itself to fancy schemes for spending money that the President disapproves of. In the past, the budget of the National Science Foundation has frequently been delayed and even emasculated simply because it is a part of the vast compendium of legislation covering the Departments of Health, Education and Welfare. This year, it is the NIH that suffers. What Congress and the Administration should acknowledge is that capricious accidents like these are not merely a guarantee of inefficient expenditure but also a great source of demoralization among scientific workers. Yet on the face of things, the way out of this kind of difficulty would seem simple enough. Even though the Department of Health, Education and Welfare is a single entity in the government (which should be broken up), is there any reason why the budgets for the several

components of the department should not be separately presented, argued over independently in Congress and then approved (or vetoed, since that seems to be President Nixon's predilection) on their own? In the old days, in the 1960s, American administrators were continually arguing over the best means of constructing a national science policy. They have rightly rejected the idea that there should be an executive department with responsibility in this field, but they should now acknowledge that the repeated muddle over important parts of the science budget is not merely an assurance that there will never be a coherent science policy but that those agencies responsible for executing scientific work will carry the burden for the government's administrative foolishness.

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100 Years Ago

Perception in the Lower Animals

As several persons seem interested in Mr. Wallace's suggestion that animals find their way home by recognising the odour of the places which they have passed whilst shut up, you may perhaps think the following little fact worth giving. Many years ago I was on a mail-coach, and as soon as we came to a public-house, the coachman pulled up for the fraction of a second. He did so when we came to a second public-house, and I then asked him the reason. He pointed to the off-hand wheeler, and said that she had been long completely blind, and she would stop at every place on the road at which she had before stopped. He had found by experience that less time was wasted by pulling up his team than by trying to drive her past the place, for she was contented with a momentary stop. After this I watched her, and it was evident that she knew exactly, before the coachman began to pull up the other horses, every public-house on the road, for she had at some time stopped at all. I think there can be little doubt that this mare recognised all these houses by her sense of smell. With respect to cats, so many cases have been recorded of their returning from a considerable distance to their homes, after having been carried away shut up in baskets, that I can hardly disbelieve them, though these stories are disbelieved by some persons. Now, as far as I have observed, cats do not possess a very acute sense of smell, and they seem to discover their prey by eyesight and by hearing. This leads me to mention another trifling fact: I sent a riding-horse by railway from Kent *via* Yarmouth, to Freshwater Bay, in the Isle of Wight. On the first day that I rode eastward, my horse, when I turned to go home, was very unwilling to return towards his stable, and he several times turned round. This led me to make repeated trials, and every time that I slackened the reins, he turned sharply round and began to trot to the eastward by a little north, which was nearly in the direction of his home in Kent. I had ridden this horse daily for several years, and he had never before behaved in this manner. My impression was that he somehow knew the direction whence he had been brought. I should state that the last stage from Yarmouth to Freshwater is almost due south, and along this road he had been ridden by my groom; but he never once showed any wish to return in this direction. I had purchased this horse several years before from a gentleman in my own neighbourhood, who had possessed him for a considerable time. Nevertheless it is possible, though far from probable, that the horse may have been born in the Isle of Wight. Even if we grant to animals a sense of the points of the compass, of which there is no evidence, how can we account, for instance, for the turtles which formerly congregated in multitudes, only at one season of the year, on the shores of the Isle of Ascension, finding their way to that speck of land in the midst of the great Atlantic Ocean?

CHARLES DARWIN

OLD WORLD

Select Committee as a Nuclear Engineer

MARKED enthusiasm for the high temperature reactor and a distinct lack of interest in the steam-generating heavy water reactor characterized the evidence of BNDC when the group appeared before the Select Committee on Science and Technology last week. British Nuclear Design and Construction is one of Britain's two nuclear consortia, the other being the Nuclear Power Group, and it is clear that their interests do not coincide.

The Nuclear Power Group was obviously eager to build a SGHWR when it gave evidence to the select committee recently (see *Nature*, **241**, 301 ; 1973), but BNDC told the committee that although the consortia has a "high opinion of the reactor's technical merits", it does not think there is much chance of selling it abroad, partly because it is "too like the light water reactors in many respects".

The high temperature reactor, according to BNDC, is another matter altogether. The first HTR could be operating in Britain by 1980, and the consortium believes it "holds out the prospect of catching up on the success of the light water reactor". Interest in France, West Germany and the United States is already high, and Gulf General Atomic of the United States has already had orders for 6 HTRs even though the company's 300 MW prototype will not be finished until the end of the year.

BNDC has already had discussions with Gulf on high temperature reactor designs, the consortium told the committee. The interest being shown in France and West Germany, allied to Britain's technical knowledge, clearly hints at the possibility of international collaboration.

But if BNDC's ideas on what type of reactor should be built to follow the as yet uncommissioned advanced gas cooled reactors differed from TNPG's, so did their ideas on the reorganization of the two consortia that Mr John Davies promised last August.

TNPG's chairman, Sir Edwin Mac-Alpine, told the Select Committee that it "would be a terrible disaster if any one company were seen to be in control" of the new design and construction company, but BNDC saw nothing wrong with an arrangement that resulted in the new company being controlled by a management contract. The rumour is that Sir Arnold Weinstock, chairman of GEC, is the man to whom

the government would like to award that contract. GEC already manages the financial side of BNDC, and Sir Hector McNeil, BNDC's chairman, was, perhaps not surprisingly, enthusiastic about the arrangement. "I think it would assist" in the running of a new company, he said. He also argued that the new consortia should be owned 51 per cent by industry, and 49 per cent by government.

But if Sir Hector fanned the select committee's fears that Sir Arnold Wein-

stock may become the doyen of Britain's nuclear construction industry, he at least calmed fears that Britain is about to buy American light water reactors, the safety of which has been much questioned of late. "I see no reason at this stage to abandon the advanced gas cooled reactor for light water reactors," he said.

Later in the week the Select Committee took evidence from Mr Christopher Layton, *chef de cabinet* to Mr Alterio Spinelli, the member of the

ENVIRONMENT

Conservation Review Complete

THE Nature Conservancy's conservation review, started in 1967, has been completed but is unlikely to be published before early 1974.

The object of the review—which has been approved by the Natural Environment Research Council but which has yet to receive the seal of the Department of Education and Science and the Department of the Environment—is to identify sites in Britain that are of national importance.

The review itself is a strictly scientific document but the object that lies behind it is to produce a coherent national conservation policy in which it is hoped government departments, local authorities, public and private landowners and industry will cooperate.

The review consists of two parts. The first is a description of the chief habitat types found in Britain and their variations. Six chief types of habitat are listed, coastland, woodland, grassland, open water, uplands and peatlands. In the second section, particular sites around Britain are described and classified into one of two grades, both of which are classified as being of national importance (the Nature Conservancy places other sites into three or four further grades of regional and local importance).

These sites are graded by applying criteria which take into account the size of the site, the diversity of its habitat, its rarity, fragility, representativeness, research and educational value, its known history, the extent to which it has been modified and its potential value if it has been damaged but is restorable. More than 400 sites are believed to be covered in the review and classified as being of national importance.

The field-work for the review was carried out by both the conservation and research sides of the conservancy. Conservation officers in the regions were best informed about known sites, but the scientific staff identified a number of others, particularly in the remoter parts of the country.

It is not intended that the review should form a once-and-for-all assessment of Britain's most important natural habitats. New sites can be added as they are identified.

The considerable delay in the publication of the review can be attributed to the government's white paper on research and development published last July. The conservation side of the Nature Conservancy is to be separated from the research side and transferred to the Department of the Environment. So much time has been spent preparing for this change (which has not yet taken place as legislation is needed) that the review has had to be put back. This has caused a certain amount of dissatisfaction in the regions as Nature Conservancy staff were working hard against a deadline eighteen months ago to finish a review that will not now see the light of day until next year. The fault is not the conservancy's. The problem lies chiefly in having to prepare for major changes and being at present answerable to two masters, the old (DES) and the new (DOE), and having to work out procedures with the latter. The DOE inevitably has to be involved although the review is purely a scientific assessment of known sites, because its policy implications are considerable. The simple publication of the document will, in itself, be a pressure for a conservation policy.

European Commission responsible for industry and technology.

Outlining the makings of a European computer policy, Mr Layton told the committee that although IBM dominates the European computer market there are specific areas where IBM can be beaten by European companies. A large company like IBM needs disciplining by effective competition, he said, and Europe must provide this, although the United States and Japanese markets will have to be penetrated if a large European computer company is to become viable.

The five leading companies in Europe are ICL, Philips, Siemens, CII and AEG-Nixdorf. Philips, Siemens and CII have already discussed the possibilities of developing a new range of computers together, and Mr Layton suggested that ICL and AEG-Nixdorf would also make a good partnership. "If ICL can find a European partner with whom it can merge effectively the commission would warmly welcome it."

Mr Layton also discussed support given the national computer companies from public funds in Britain, France and West Germany. Such support is clearly against the spirit and letter of the Treaty of Rome, he said, but "in fact the aids are tolerated by the commission and protective national procurement practices continue at the present time". This situation cannot continue indefinitely and the question is whether the national preferential policies are to be replaced by a community preferential policy—at least for a time. Massive government support in the form of orders accounts for IBM's success in the United States, and without this support Mr Layton does not believe the European national companies would be viable.

ESRO

Choosing the Next Step

from a Correspondent

THE European Space Research Organization is to decide by the end of this month which satellite to launch later this decade to follow COS-B and GEOS. The three options—only one of which will be chosen this month although the others may be added later—were presented at a lively symposium in Frascati last week to a wide selection of European scientists.

The Venus orbiter would investigate the atmosphere and surface of Venus, HELOS (Highly Eccentric Lunar Occultation Satellite) would provide observations of X-ray sources, and the mother–daughter projects would study the earth's magnetosphere and the adjacent regions of interplanetary space.

The Venus orbiter mission would link up with NASA's proposed biennial Venus project which includes a probe that will explore the Venusian atmosphere. The orbiter would be provided by ESRO and the experiments selected by a joint NASA/ESRO team. Venus is of particular interest to geophysicists as its mass and radius are the closest of all the planets to those of the Earth. It is also hoped that studies of the comparatively simple circulation patterns in the atmosphere of Venus will lead to a greater understanding of the more complex circulation patterns on Earth.

The original concept of the HELOS mission (see *Nature*, **228**, 756 ; 1970) used moon occultations to obtain positions and structures of X-ray sources with high precision. An off-set mode now offers the additional capability of making continuous observations over periods of many hours. Variable X-ray sources can thus be observed from a satellite, which because of its eccentric orbit, does not suffer from the frequent interruptions of the radiation belt and Earth occultations as it would be in a near Earth orbit. HELOS is a purely European project complementary to NASA's X-ray programme. However there are now difficulties in the funding of NASA's high energy atronomical observatory in the late 1970s.

The mother–daughter project involves the launch of two satellites on one Thor Delta rocket. They will be launched in conjunction with NASA's IMP programme to combine with its heliocentric satellite which will be in solar orbit close to the libration point at 250 Earth radii. These missions should increase the understanding of the physics of the magnetized plasma in which the Earth is embedded. The multiple satellite mission will help unravel the spatial and temporal variations of the radiation belt, the magnetopause, the bow shock and magnetotail. When the mother and daughter are within the magnetosphere the heliocentric spacecraft will act as the monitor of the solar wind and thus establish the relationship between such phenomena as substorms with changes in the solar wind.

The launch dates for the three satellites if they are chosen later this month are mid-1977 for the mother–daughter satellite, mid-1978 for the Venus orbiter and the end of 1977 for HELOS. Estimates of the costs of the three satellites are not yet available.

COMPUTERS

No Freeze

THE Computer Board for Universities and Research Councils spent £9.3 million in 1971–72, a twenty-six per cent increase over the previous year. Not only did the expenditure go up by this amount but the spending in 1971–72 was almost £200,000 less than the board allocated for the year. Of this total £6.23 million was spent on hardware, £2.7 million on recurrent costs and only £0.38 million on buildings (Cmnd. 5220, HMSO, £0.16).

Computer capacity in British universities is now ten times greater than it was in 1965, and the board estimates that by March 1974 more than twenty-five times the 1965 capacity will be available —a growth rate of about 40 per cent a year. But the board says that this increase is only a lower estimate of the available running time chiefly because the quality of computer performance has increased during the past decade and users now have better access to the facilities.

During the past two years, the Computer Board has authorized the buying of eighteen new computers of which twelve have already been delivered. The new installations include the CDC 7600 at the University of London which is also providing facilities for other universities in the south-east of England, the CDC 7600 and its linked partner the ICL 1906A at the University of Manchester, the 1906A computers installed at the Universities of Birmingham, Leeds, Nottingham and Oxford and the IBM 370/165 at the University of Cambridge. The Cambridge machine is the only IBM machine installed recently, and the board says that the

choice was influenced to a great extent by the Cambridge argument that it needed a computer that would be compatible with the many overseas universities and research institutes which have equipment—so that computer programmes could easily be interchanged—and also so that the system would be compatible with the IBM facilities at the Medical Research Council's Molecular Biology Laboratory at Cambridge. As its part of the bargain, the MRC agreed to contribute £160,000 to the capital cost and £20,000 a year to the recurrent costs of the installation in return for ten per cent of the running time. Also, the Cambridge machine will be available "for a substantial proportion of time" to users from other universities who need time on an IBM machine. The board states that the arrangements for such allocations are under consideration although twenty per cent of the time has been set as a tentative limit.

Since the Computer Board was set up in 1966 it has spent £18.8 million on ICL computers, £4.95 million on IBM computers, £9.0 million on CDC computers, £290,000 on DEC machines and £150,000 on computers from other manufacturers. By far the biggest sum spent on IBM machines has been the £1.75 million spent on the 370/165 at Cambridge while the CDC 7600 at the University of Manchester cost £2.23 million. The largest single contract for an ICL machine was also placed at Manchester for the 1906A, the linked partner of the CDC 7600.

Five ICL 1906A computers have been provided by the Computer Board in the past two years and the users of these machines, together with ICL, have set up a Software Steering Committee to identify developments required to improve the performance of the computers, and subsequently to implement the developments. These universities have also, in collaboration with the Science Research Council's Atlas Computer Laboratory at Chilton, set up a library of mathematical routines. Since the first edition of this library was released in October 1971 the board has encouraged the group to make the library more generally available. The eventual aim of the group and the board is to establish a master library which is independent of the machine.

WORLD HEALTH ORGANIZATION

Problems of Age

Two recent reports from the World Health Organization highlight the need for treatment for diseases which are on the increase in the world today. In the first report, *Drug Therapy for Cancer*, by G. Brule, S. J. Eckhardt, T. C. Hall and A. Winkler, the authors point out that in many parts of the world surgical and radiotherapeutical methods of treating cancer are simply not available and treatment by drugs, chemotherapy, is therefore becoming much more important. In the other report, *Psychogeriatrics* (WHO Technical Report No 507), a warning is given that the increased longevity of people is leading to an increase in mental diseases but that not enough is being done to cater for these people.

The ever-increasing presence of carcinogens in the environment combined with a population that is becoming older means that cancer will be an increasing problem, in spite of the fact that effective treatment for many forms of the disease is now available. But in the developing countries there are few facilities for treatment except by giving drugs. The role of chemotherapy is therefore of greater importance in these countries than it is in the developed countries where other forms of treatment are available. It is fortunate that the treatment of cancer by drugs is one of the great developments of the past fifty years.

At present hundreds of drugs are tested every year to see whether they are suitable for use in combating tumours. The introduction of community programmes to screen for certain diseases has meant in recent years that effective drugs can be identified much more easily than in the past. Of the many drugs tested, however, only a few have been accepted and the report pleads that doctors and medical health advisers in countries where chemotherapy is the only possible method of treatment should be made aware of what drugs are available and how efficient they are in treating cancer.

The report includes a documentation of drugs that are available and an account of their efficacy and how they should be administered. The emphasis in the report is on the practical side of treatment for cancer and the World Health Organization hopes that as well as being suitable for both undergraduate and postgraduate education the report will prove helpful to the practitioner who is faced with difficult problems of what particular drug to prescribe for treating cancer.

The second report, although on a different disease, has also arisen chiefly because of the increasing longevity of people. An increased expectation of life means an increased expectancy of mental illness, which becomes progressively more common as people grow older due in part to detrimental changes in the brain and its blood vessels.

The report, however, is written in a partial vacuum in that there is an inadequacy of epidemiological data of psychiatric diseases of old people. The report urgently calls for more data and also for a study of currently available services for treating the mentally ill and the pattern of use of such facilities.

In the past, according to the report, many psychiatric illnesses of old age have not been recorded as such and so the magnitude of the problem has, in general, been underestimated with only the most severe psychoses and dementia being noted.

As part of the plan to study the problem the report recommends that an operational research exercise be carried out to define the merits of keeping old people in institutions compared with keeping them at home or in community centres. In such a study the effects on the other members of the family should be taken into consideration. It is also pointed out that early screening programmes could help in alleviating the difficulties of solving problems associated with old people whose mental health has failed.

Royal Society Exchange

SINO-BRITISH scientific collaboration is going from strength to strength. Later this month, three British scientists will visit China for between two and three weeks, a visit which reciprocates that made to Britain last October by a seven man delegation of Chinese scientists (see *Nature*, **239**, 245 ; 1972).

The present round of visits was initiated in May 1972 by Sir Alan Hodgkin, President of the Royal Society, who went to China with Sir Kingsley Dunham and Sir David Martin. Until then there had been no regular visits between the countries since the cultural revolution of the mid 1960s.

The present visits will be undertaken by Professor R. L. Wain of the agricultural chemistry department at Wye College, University of London, Dr F. L. Rose of the pharmaceutical division at Imperial Chemical Industries and Professor G. Allen of the chemical physics department at the University of Manchester.

During their stay in China, Professor Wain and his colleagues, who will travel independently and spend differing times in the country, will follow programmes arranged for them by the Academia Sinica. They will visit laboratories in Peking, Shanghai and Canton, and will lecture as well as discuss their work with Chinese scientists. The visits will coincide with the British Industrial Technology Exhibition in Peking.

NEW WORLD

Congress Backs Down on NIH Budget

by our Washington Correspondent

CONGRESS has finally given up its attempts to pass an appropriations bill for the Department of Health, Education and Welfare which is acceptable to President Nixon. With only four months of the present fiscal year left to run, both the House and the Senate last week reluctantly decided to extend until June 30 the arrangements under which HEW has been operating for the past eight months. The upshot is that the Administration will simply fund the agencies of HEW, which include the National Institutes of Health, at a level considerably lower than Congress wishes.

The long struggle between Congress and the White House over the HEW budget is just one facet of the bitter dispute which is now raging over which branch of government should have final control over the pursestrings, but it is a struggle which particularly concerns the scientific community since the HEW budget contains the bulk of the federal government's expenditures on biomedical research.

Last year, the HEW budget became an election year political football, with Congress twice passing measures which President Nixon vetoed as inflationary. Finally, in the dying days of the last session of Congress in October, a continuing resolution was passed which allowed HEW to receive funds until February 28. The idea was that when Congress reassembled in January, it would have another crack at drawing up a budget for the department which would either be acceptable to President Nixon in his present parsimonious mood, or which would have sufficient support on Capitol Hill to allow a presidential veto to be overridden.

But last week, Congress backed down and simply extended the continuing resolution for the rest of this fiscal year. Explaining why the appropriations committees decided not to try for another bill early in this session, Mr Daniel Flood, chairman of the appropriations subcommittee which deals with the HEW budget said "frankly, our committee believes that an attempt to enact a third bill would be a wasted effort. It seems very unlikely that a bill which would be acceptable to a majority of the Congress would also be acceptable to the President". He also pointed out that it is now time for Congress to start work on the 1974 appropriations bill.

The continuing resolution, in short, provides authority for the Administration to spend money on HEW programmes up to the lowest level for individual items contained in either of the separate appropriations bills passed by the House and the Senate last June. The resolution thus allows the Administration to spend up to about $28,000 million this fiscal year through HEW. But even this amount, which is some $600 million less than the first vetoed bill entailed, is still more than $1,000 million greater than President Nixon's original budget request of $26,800 for HEW. Moreover, at the end of last year, when Congress was trying to ram through an appropriations bill increasing President Nixon's budget request, the Office of Management and Budget was busy revising the request downwards, and in January this year the OMB proposed a revised budget for HEW of $26,100 million.

The irony of the whole business is that it makes no difference what level of funding Congress finally decided upon, since the Administration will spend only as much as it wishes. In other cases in which Congress has tried to increase budgets this fiscal year, the Administration has simply impounded some of the appropriated funds and Senator Norris Cotton of New Hampshire, speaking for the Administration last week, said that "if this continuing resolution should pass in its present form, it is the purpose of the Department of Health, Education and Welfare, for the remainder of the year, to make its expenditures on the basis of the President's revised budget of $26,100 million". That, of course, is what Congress is getting angry about.

UNIVERSITIES

Free Speech in California

by our Washington Correspondent

CHARLES SCHWARTZ, a professor of physics at the University of California at Berkeley, has won a lawsuit against the Lawrence Berkeley Laboratory on the grounds that he has been refused summer employment because of his radical political activities. The court ruled that such activities are constitutionally protected, and directed the laboratory to compensate him for loss of salary. The ruling is the latest, and perhaps the final, step in a dispute between Schwartz and the laboratory's management over the question of whether scientists should be allowed to take part in political activities on the laboratory's premises in their free time.

The issue was first raised in the autumn of 1969, when political activism was at its height on university campuses throughout the United States. At that time, a group of scientists at the laboratory proposed holding lunchtime political discussions about the Vietnam war, but their proposal was vetoed by Dr. E. M. McMillan, the laboratory director. McMillan later appointed a committee to examine the laboratory's policies with respect to political activities on the campus, and in March the following year, the committee backed McMillan's actions in excluding political meetings from the laboratory.

Later that year, however, Schwartz, who was employed by the laboratory during the summer, held two lunchtime seminars in defiance of the ban on meetings, and was promptly suspended for two weeks, a sentence which was later reduced to two days. The following year, Schwartz was informed that his request for summer employment had been denied, and he immediately filed complaint with the faculty Committee on Privilege and Tenure. When the committee failed to find fault with McMillan's action, Schwartz appealed to the Academic Freedom Committee, the President of the University and the Board of Regents, all to no avail. Finally, the local branch of the American Federation of Teachers took the case to court, the upshot of which was Schwartz's victory last week. While the legal dispute was going on, however, McMillan announced a new policy at the laboratory allowing complete freedom of speech.

Schwartz, who is very much a radical thorn in the University of California's flesh, promptly accused the administration of the University of California at Berkeley of not living up to its dedication to free speech by backing up his fight with the laboratory management. His victory may, however, be shortlived, because the court ruling included the statement that "this decision should not be construed as affecting future summer job placement opportunities for petitioner which may be dictated by budgetary considerations".

What does all this mean for NIH? The short answer is that every institute will have a smaller budget this year than last, apart from the National Cancer Institute and the National Heart and Lung Institute, which will get modest increases. Moreover, there will be large cutbacks in health manpower education and training. In contrast, President Nixon's original budget request, made before the cutbacks in overall federal spending late last year, would have increased the budgets of all agencies, and the vetoed bills would have provided them with a veritable bonanza.

One effect of the financial stringencies in NIH is that the amount of money available for new grants will be particularly tight. According to an item in the newsletter *Science and Government Report,* many of the NIH noncompetitive grants—those used to fund projects over several years—will be cut back to make more money available to support new projects. The result will be that researchers who have embarked on long-term projects with NIH funding will be given less money than originally promised.

President Nixon's budget request for next year entails even less expenditure for many HEW programmes—including most institutes in NIH—than his revised budget for this year. There is thus clearly going to be another protracted fight between Congress and the White House over funds for health and social programmes. If this year's fiasco is any guide, however, President Nixon is likely to get his way in the end.

BUDGETS

Light in the Gloom

by our Washington Correspondent

AMID the gloom and despondency in the scientific community following publication of the Administration's austere budget for 1974 and the dismantling of the White House science policy machinery, a report published by the Battelle Memorial Institute sticks out like a sore thumb. The institute reckons that total expenditures on science and technology in the United States will amount to about $30,100 million in the calendar year 1973, which would represent an increase of 7.5 per cent compared with estimated outlays in 1972. The forecast predicts that the chief increase will come from industry, but it also suggests that "Federal support has begun what could be a sustained rise".

The institute's optimism will certainly be regarded with some surprise by those scientists who have had their budgets cut or their projects terminated as a result of cutbacks in spending by the Administration, but the report nevertheless suggests that federal spending

on science and technology will climb to about $16,300 million this year, compared with $15,200 million last year ; spending by industry is predicted to increase from $11,320 million last year to about $12,200 million this year. The remainder will come from academic and non-profit institutions, which are expected to increase their expenditures on research and development slightly.

The forecast for federal spending is based on recent trends in budgets, which the report suggests is "somewhat safer than reliance on recently published figures". Nevertheless, the most recently published figures—the Administration's budget proposals—suggest that federal spending on science and technology in the 1973 fiscal year (which runs from July 1972 to June 1973) will be about $15,900 million, an absolute decline of some $200 million from the last fiscal year. Since the Battelle forecast is for the 1973 calendar year, this sharp but perhaps temporary cutback in overall federal spending in the 1973 fiscal year does not show up in the optimistic figures given in the report.

As for patterns of expenditure, the forecast notes that there has been a shift away from military, nuclear and space research towards civilian science and technology, but it also warns that "in longer term overall dollars, this shift is still not as significant as many believe". The predicted increase in industrially funded research and development follows partly from an expected increase in corporate sales.

A year ago, the Battelle Memorial Institute predicted that total expenditures on science and technology would begin to increase after a period of stagnation, but warned that the full impact of the upturn might be delayed. That, indeed, is what has happened—the institute predicted last year that spending on research and development would reach $30,100 million in 1972, but it actually reached only about $28,000 million, and the institute is now repeating for 1973 the prediction it made for 1972.

SCIENCE POLICY

Nixon Gets His Way

by our Washington Correspondent

PRESIDENT Nixon now seems almost certain to get away with his plans for scrapping the Office of Science and Technology without running into opposition from Congress. Hearings held independently by House and Senate Government Operations subcommittees last week brought out the fact that isolated outbreaks of sharp words and the general air of disquiet among many scientists over the plans do not give the committees sufficient reason to be difficult about them. Congress has until April 6 to pass a resolution disapproving

the plans, but so far, no disapproving resolution has been introduced.

The hearings last week were chiefly a formality, and provided a forum for Fred Malek, deputy director of the Office of Management and Budget, and Dr H. Guyford Stever, director of the National Science Foundation, to reiterate the Administration's thinking. The reorganisation plan (see *Nature,* **241**, 234 ; 1973) involves scrapping the Office of Science and Technology and the post of Science Adviser to the President, and transferring to the Director of the National Science Foundation some of the responsibilities for advising the president on science policy.

Both Senator Abraham Ribicoff, chairman of the Senate Government Operations subcommittee, and Chet Hollifield, his counterpart in the House of Representatives, noted that the plan has been criticised as downgrading scientific advice in the Administration— Dr Stever, unlike previous Science Advisers to the President, will advise not the president, but Dr George Shultz, Secretary of the Treasury and Presidential Assistant for economic affairs. Malek replied that the National Science Foundation has more staff to perform science policy analyses than could possibly exist in the White House, and that "Dr Stever will have ready access to the President's closest advisers."

Apart from the question of downgrading advice, members of the House subcommittee were a little concerned that no increase in budget or staff has been given to the National Science Foundation to enable it to perform its new role, but Malek simply said that it is his feeling that "the new NSF budget, with the number of people and resources that they have, will be sufficient to absorb this added capacity". In other words, the foundation will have to carry out its new responsibilities with money and people originally required for other purposes.

The most outspoken criticism of the plans last week came from Mr John Davis, chairman of the House Subcommittee on Science, Research and Development. In a statement presented to the Government Operations subcommittee, Davis expressed alarm at the scrapping of OST and concern about the present state of US science and technology in general. He pointed out that the United States has a balance of payments deficit in high technology products, and that in terms of percentage of gross national product, the US spends about half as much on research and development as Japan and West Germany, the two chief exporters of high technology products to the United States. In such a situation, Davis suggests that "the abolition of OST and a downgrading of our scientific apparatus seems counterproductive".

NEWS AND VIEWS

T-Mycoplasmas and Reproductive Failure

ATTENTION was drawn recently (see *Nature*, **241**, 425 ; 1973) to the significant relationship between maternal infection and foetal loss and morbidity. Rubella, cytomegalic inclusion disease and toxoplasmosis were all cited as causing retardation of human foetal growth and reference was made to further evidence, pointing to the possible implication of Coxsackie viruses in retardation of foetal growth and certain congenital malformations, particularly those affecting the heart. Low birth weight has been attributed to human maternal infection with T-mycoplasmas (Braun and colleagues, *New Engl. J. Med.*, **284**, 167 ; 1971), and these organisms have been isolated from the foetal membranes in cases of repeated abortion (Kundsin and colleagues, *Science*, **157**, 1573 ; 1967).

Mycoplasmas, which used to be known as pleuropneumonia-like organisms, are the smallest free-living organisms, with similarities to both viruses and bacteria. They resemble viruses in size, and are therefore ultrafiltrable, as well as in having no rigid cell wall. They resemble bacteria in their ability to grow in acellular media ; in their chemical composition which includes both RNA and DNA and in their growth being inhibited by tetracyclines and some other antibiotics which interfere with their metabolism. A feature of the T-strains is their ability to metabolize arginine or urea with the production of ammonia (see *Lancet*, ii, 248 ; 1967). Mycoplasmas have been implicated in a wide variety of human diseases including primary atypical pneumonia (Channock and colleagues, *Proc. US Nat. Acad. Sci.*, **48**, 41 ; 1962), myringitis, otitis media, various rashes, erythema multiforme, the Brodie-Reiter syndrome and, in the case of the T-strain, non-specific urethritis.

On page 120 of this issue of *Nature*, H. Gnarpe and J. Friberg of the University of Uppsala present evidence that T-mycoplasmas may be a possible cause of human reproductive failure. All who have had experience of the diagnosis and treatment of human infertility are well aware of the not infrequent couples who, after full conventional investigation, fail to present any explanation for their continued reproductive failure. Emotional factors, immunological causes and mysterious "infections" are among the possibilities that the groping clinician postulates as a cover-up for his ignorance and his inability to account satisfactorily for the continuing infertility.

It is just such a group of patients that Gnarpe and Friberg have studied, having eliminated the common causes of reproductive failure by conventional clinical investigations. They were able to isolate T-mycoplasmas from 89 per cent of the hundred and four patients (from the seminal fluid of forty-five of the husbands and from the cervical mucus of forty-seven of the wives). By contrast, T-mycoplasmas were isolated from the cervical mucus of only nine of forty pregnant women and from the seminal fluid of six of twenty-three men married to women who were pregnant or who had recently delivered. The difference in the incidence of T-mycoplasmas between the fertile and infertile patients is highly significant. Treatment with doxycycline was shown to eliminate T-mycoplasmas from all of ten men and nine of eleven women. Within five months of eradication of T-mycoplasmas 29 per cent of the infertile women had conceived, no pregnancies having occurred in a preceding 3-months' period of observation.

These findings are of great interest and would certainly seem to justify the further investigations which the authors are carrying out. Perhaps two comments might be justifiable. In the first place, it is possible that the much lower incidence of T-mycoplasmas found in pregnant women and their husbands could be attributable to the pregnancy —and it should not be difficult to refute this suggestion if untrue. In the second place, the restoration of fertility by treatment could have been more convincingly demonstrated if a double blind trial of therapy had been carried out, because it is not impossible that psychotherapeutic factors may have been involved.

G. I. M. S.

Ubiquitous Neutrinos

DURING the past year neutrinos seem to have become a panacea for many of astronomy's ills. So little is known about the physical properties of these elusive particles that, as many astrophysicists (and geophysicists) are coming to realize, the visible manifestations they produce in different models can be adjusted to cover a multitude of sins by suitable tinkering with, for example, the hypothetical mass and equally hypothetical lifetime of the neutrino.

In January last year Bahcall, Cabibbo and Yahil published a discussion of the stability of the neutrino in which they pointed out that "our present knowledge of neutrinos is insufficient to establish whether or not neutrinos are stable" (*Phys. Rev. Lett.*, **28**, 316 ; 1972). The point, of course, is that the very low counting rate reported from solar neutrino detectors implies that neutrinos are very stable particles. If they have finite mass they could be unstable, and Bahcall *et al.* showed that this could still be consistent with the solar neutrino experimental results.

But what is really meant by stability in this case? All that is really "known" from those experiments is that a solar neutrino, with typical energy 1 MeV, lives long enough to travel the distance between the Earth and Sun at the speed of light—that is, for 500 s. But even this evidence could be the result of misinterpreting the data. According to Bahcall *et al.*, standard astrophysical models of the Sun could be incorrect, so that neutrinos are not produced in the amounts predicted. Alternatively, the solar models may be correct, but the neutrinos produced decay before they reach Earth. Either effect could explain

the discrepancy between theory and observation. Several articles published in *Nature* and *Nature Physical Science* recently have explored the consequences of the first proposal, suggesting, among other things, that repeated sudden mixing in the Sun's core could be associated with the temperature changes that produced ice ages on Earth.

But what of the second possibility? Once it is assumed that neutrinos from the Sun do decay, the flux of neutrinos near the Earth is a very sensitive function of energy, and there are even more parameters which can be adjusted. Hamza and Beck have suggested (*Nature*, **240**, 343 ; 1972) that the adjustments allowed might be drastic enough to encourage speculation about the role of neutrinos produced by radioactive decays within the Earth itself.

Experiments reveal that the neutrino is stable over about 10^4 cm, and if the solar neutrino decay hypothesis is correct the neutrino decays within about 10^{13} cm. By choosing a range of 100 m, energy from radionucleide decay in the form of neutrinos is certainly kept within the Earth's crust instead of being lost ; a stable path length of 300 km is better from a geophysical point of view, say Hamza and Beck, because the energy from the neutrinos would be released in the form of heat at a range of depths around 300 km, where there is "a well known second order seismic discontinuity", hitherto unexplained.

The latest development in the speculative flight of neutrino fancy comes from Cowsik and McClelland, who follow up the implications of the positive mass required to allow neutrinos to decay (*Astrophys. J.*, **180**, 7 ; 1973). They consider the evolution of a big-bang universe in which many such neutrinos were produced before the time when radiation and matter decoupled. Unlike other particles, neutrinos to a large degree survive annihilation as the Universe expands, because of their small cross-sections for interaction. The number density decreases only with increasing volume of the Universe, say Cowsik and Mc-Clelland (who seem to be trying to both have their cake and eat it, for their neutrinos certainly do not decay in 10^2 cm, or even 10^{13} cm ; but that is quite within the rules of the neutrino game as long as one does not pretend to solve all astrophysical problems at once). A mass for the neutrino of 2.5 eV/c^2 is well within the best experimental limit yet obtained (<60 eV/c^2), and according to Cowsik and McClelland this would be sufficient for the gravitational influence of the sea of neutrinos throughout space to close the Universe.

That is a happy thought for those cosmologists who would like the Universe to be closed. But it is possible to go still further. With a neutrino mass of a few eV/c^2 neutrinos would be by far the dominant gravitational influence in the Universe. Could the growth of galaxies and clusters of galaxies have been triggered by gravitational interactions of neutrino clouds? There is certainly a long-standing discrepancy between the masses needed to bind many clusters of galaxies together and the total mass obtained by summing the masses of individual galaxies, estimated according to the best astrophysical theories.

Cowsik and McClelland have looked in detail at the case of the Coma cluster, a well known example of the "missing mass" dilemma. Treating neutrinos as a Fermi-Dirac gas now at zero temperature, the mass of each neutrino in the cloud must be about 2 eV/c^2, with a total mass of 4×10^{49} g, if the cluster is to be bound. The distribution of mass within the resulting potential well happily fits the observed central peak and extended tail seen in the distribution of visible galaxies in the Coma cluster ; as such a well develops, whatever its origin, neutrino quantum states are progressively drawn in so the neutrinos fill the well. Neutrinos of mass 2 to 3 eV/c^2 can, it seems, close the Universe and bind the Coma cluster.

Should all this be taken seriously? Certainly not. After all, the various intriguing neutrino models are not consistent with one another. Whether one of the suggestions should be taken seriously is another question, to be answered, perhaps, in accordance with whichever problem seems the most baffling. With neutrinos, it seems, one can solve some of the problems most of the time, and most of the problems some of the time. But it does not seem possible to solve all of the problems all of the time. Alas, the panacea is not universal after all.

By our Cosmology Correspondent

Drift in the Ionosphere

IF the physical and chemical parameters of the F region of the Earth's atmosphere could be measured more accurately, understanding of it would increase enormously. A great many processes affect this region and the task of sorting these out is hampered by the large uncertainties in the measured parameters and also the striking lack of data. One of the chief examples of this is the measurement of wind velocities in the F region. Many experiments measure only a single component of the velocity whereas the accurate measurement of the components parallel and perpendicular to the Earth's magnetic field are vital to the discovery of the underlying causes of these winds.

The F region lies between heights of 170 and 1,000 km and is the most densely ionized of the ionospheric layers, having an electron density of 10^{12} m^{-3}. It is formed by the ionization of atomic oxygen by solar X-rays. One of the peculiarities of the F region is known as the geomagnetic anomaly. Unlike the lower C, D and E regions the electron density at a specific height in the F region is not constant but varies as a function of geomagnetic latitude. Also the maximum electron density does not seem to be related to the angle of arrival of the Sun's rays as is the case for the other layers. Many suggestions have been put forward to explain these anomalies. Perhaps the loss rate changes because of variations in the concentration of atomic oxygen ; alternatively fluctuation in the upper atmospheric temperature may affect the reaction constant ; or maybe energetic particles leaking from the magnetosphere produce ionization at certain latitudes ; or possibly the anomalies are caused by a movement of the ionospheric plasma, this being caused by winds in the neutral atmosphere and electric fields originating lower in the ionosphere. Now the observed anomalies could be caused by one or more of the above phenomena but there seems to be little doubt that bodily movements of the atmosphere are responsible for part of the anomalous behaviour. The careful study and measurement of the magnitude and direction of these winds are, therefore, very important.

Three methods are being used at present. The chemical trail method relies on a rocket to release a chemical, usually barium or sodium, into the ionospheric region. The

drifting of the resulting chemical trail is then observed from the ground. This technique has certain drawbacks—the trail only lasts for a few minutes, the experiment can only be carried out on clear nights, the maximum height is 200 km and, finally, rockets are expensive. The results, though, are unambiguous and accurate.

A close-spaced antenna system can also be used to measure ionospheric drifts. The ionosphere is illuminated with radio waves from the ground or from a geostationary satellite or a radio star and the diffraction pattern of the reflected or transmitted waves on the ground is then monitored. Changes in this pattern are related to the ionospheric drifts. Many problems, however, arise in the interpretation of the changing patterns and it is now thought that the results only refer to moving fluctuations in the electron density and not to movements of the whole ionospheric region.

A new and very exciting method of measuring ionospheric winds uses observations of incoherent scattering from electrons. An electromagnetic wave falling on a free electron causes it to oscillate and thus to radiate a scattered wave in all directions. This last sentence immediately reveals two of the problems encountered when using this Thomson scattering method to probe the ionosphere. First, electrons are very small (they have scattering cross-sections of 10^{-28} m²) so very little power is reflected from an ionized layer. For example a scattering volume with the dimensions of a cube of sides 100 km, centred on the maximum of the F layer where the electron concentration is about 10^{12} m⁻³, has a total scattering cross-section of about 10^{-1} m². It is the power returning from this effective area, placed at a distance of several hundred kilometres, that has to be measured.

Second, as the scattered wave is radiated in all directions, the scattered power returning to the ground is minute. By using a very powerful transmitter (several tens of kilowatts mean power) these problems can be overcome and with sensitive spaced receivers coupled to narrow-beam directional aerials the electron density as a function of height can be measured. If the Doppler shift of the reflected signal is also observed the line-of-sight velocity of the electrons can be found. Analysis of the spec-

trum of the returned pulse also gives the electron and ion temperature of the region.

Those who used this technique previously only operated one receiver and thus only measured a single component of the velocity at any one time. A complete picture is built up by observing different points of the ionosphere at different times. The big drawback of this method is that spatial and temporal variations can not be distinguished. Preliminary results of the first spatio-temporally coherent measurements of electron densities and velocities using the Thomson scattering method are set out on page 109 of this issue of Nature. Taylor, Rishbeth and Williams achieved this by using the Malvern radio transmitter and receivers at Aberystwyth, Jodrell Bank and Chilbolton; the receivers were each about 110 km away from the transmitter. The beam width of the receiver aerials was 2°, giving a height resolution of 13 km in the E region

and 40 km in the F region. Simultaneous measurements were made of the same scattering volume, this being vertically above Malvern. The electron velocity can be measured to an accuracy of ± 12 m s⁻¹, and by spectrally analysing the returned signal the electron and ion temperature at a specific height can be found to an accuracy of ± 15 K. These sensitivities compare favourably with the chemical trail observations but the great advantage of this incoherent scatter system is its relative cheapness and the fact that it can be run continuously.

Theorists will anxiously await more data from this group. A series of accurate observations of F layer densities, winds and temperatures and their variations with the time of day and the season of the year should provide the long-awaited key to an understanding of this mystifying region of the atmosphere.

D. W. H.

Recruitment of Cells in an Autoimmune Response

THE concept of tolerance originated from the observation by R. D. Owen (Science, 102, 400 ; 1945) that in some dizygotic twins in cattle, erythrocytes of two antigenically different kinds could be found. The explanation, which emerged later from the work of Burnet and Fenner, was that during foetal life self recognition occurred after which a state of self tolerance pertained. In the cattle twins it was supposed that exchange of cells occurred as a result of placental fusion before the self recognition had taken place and that later the foreign cells became accepted and tolerated as self entities. Part of the early theory underlying this process was that self-reactive clones of cells were eliminated from the body. Tolerance on such a basis would involve the absence of any cells capable of reacting against a tolerated antigen. In recent years this general notion has been challenged. The communication by Cohen in next Wednesday's Nature New Biology (March 14) continues this questioning.

Earlier studies from the Weizmann Institute have shown that certain populations of rat lymphocytes, when grown on syngeneic fibroblast monolayers in vitro, can develop a cytotoxic capacity against the fibroblasts. This cytotoxicity can be blocked by the addition of syngeneic serum. Injection of lymphocytes sensitized on syngeneic fibroblasts into the foot pads of syngeneic recipients leads to enlargement of the draining lymph nodes. The interpretation of these

experiments is that there exist in normal rats cells capable of undergoing autosensitization but that this is usually blocked by serum factors. Once, however, the sensitization process has occurred then the activated cells can have a cytotoxic autoimmune effect. Cohen addresses himself in the latest series of experiments to the question of the source of the cells in the enlarged lymph nodes which follow injection of syngeneically sensitized lymphocytes into a syngeneic recipient. Irradiation of the donor cells after sensitization did not much reduce the lymph node swelling whereas irradiation of the host did. The cells in the lymph node were only markedly cytotoxic when swelling had occurred and Cohen is inclined to the notion that recruitment of autoimmune cytotoxic cells from the host is brought about by the injected donor cells.

It could be argued that the syngeneic fibroblasts in vitro have a neo-antigen because of their existence in culture, but it is difficult to see on this basis why the sensitized cells should react against an antigen in vivo which should not be there. Alternatively it might be thought that the sensitized cells were themselves antigenic and that the predominantly host response was against the grafted donor cells. Again it is difficult to see why the induced response of host cells should be able to operate against fibroblasts in vitro. Whatever the final resolution of these arguments the experiments are ingenious and deserve attention.

BIOMETRICS
Disease Inheritance

from a Correspondent

MULTIFACTORIAL models for the inheritance of liability to disease was the subject of a symposium held in London on February 15 and organized by the British Region of the International Biometric Society.

Some diseases are known to be caused by a single recessive gene. If this gene causes death before adulthood, then the parents of an affected child must both be heterozygous for the gene and hence the risk of the disease for any other child they bear is one in four. Many diseases seem to have a genetic component but not to be inherited in this simple way. Only a proportion of the individuals homozygous for the recessive gene may have the disease and some individuals not homozygous for the recessive gene may have it. The multifactorial model assumes that there are many genetic loci and many environmental factors involved in the causation of the disease.

Professor D. S. Falconer (University of Edinburgh) reviewed the development of the threshold model and his own work on diabetes. In the threshold model, each person has a liability to disease that can be measured on some continuous scale. The individual succumbs to the disease if his liability exceeds some threshold value. The threshold may depend on sex and age. The liability is inherited in the same way as other continuous characters. The idea of an abrupt threshold may be biologically unacceptable but the threshold model is mathematically equivalent to a more realistic model in which some underlying variable takes different values for different individuals, correlated for relatives, and the probability of having the disease is a sigmoid function of this underlying variable. The parameters of the model are estimated from the incidence of the disease in the general population and the incidence of the disease in relatives of the affected individuals. Making some genetic assumptions, the model can be used to calculate risks for other types of relatives of the affected individuals.

Dr C. Smith (University of Edinburgh) discussed approximate and exact methods for computing risks when information is available for a number of relatives of an individual. Professor Falconer and Dr Smith discussed the evidence for a multifactorial determination of certain diseases. Dr Smith commented on the difficulties of distinguishing, on the basis of data on disease incidence, between models involving a single genetic locus and multifactorial models involving many loci.

Dr C. O. Carter (MRC Clinical Genetics Unit, London) presented evidence, including some concerning sex differences in disease incidence, for the multifactorial determination of some common congenital malformations, such as harelip and cleft palate. He argued that the complex nature of foetal development and the prevalence of genetic polymorphisms support a polygenic model rather than a single gene model with low penetrance. The polygenic model gives a better fit to data on low frequency malformations. For higher frequency malformations the polygenic model is less easy to verify but the single locus model, together with the low fitness of parents, would imply a very high level of mutation.

Professor J. H. Edwards (University of Birmingham) argued that the multifactorial model may be used deductively to calculate recurrence risks but is of no use for the inductive development of more soundly based explanatory models. He saw future progress coming from an increased understanding of the basic but complex genetic determinants of the disease. He stressed, as did the other speakers, the dangers of always interpreting familial correlations as attributable to heredity rather than environment. In the discussion the possibility of virus transmission being a chief cause of familial correlations was mentioned.

The complexities arising from a range of patterns of causation even of a single disease were not discussed in detail. There was very little discussion of possible deficiencies in the data used to estimate disease incidence. The difficulty in discriminating between different models of inheritance has an advantage in a certain robustness of the predictions from any model to the inadequacies of that model. The real questions concern the extent to which empirical data can be extrapolated to predict risks for more distant relatives and the extent to which more complex family data can be used to improve these predictions. When does the extrapolation give better estimates than available empirical data?

Dr Smith mentioned recent work on the use of values of a trait correlated with the underlying variables to improve the prediction of risk. This may increase understanding of the nature of the underlying variable. There can be no argument that statistical models are only a substitute for a more basic understanding. There will be different estimates of how long it will be before statistical models for disease inheritance are no longer necessary.

INSECT HORMONES
Ecdysone Problems

from our Insect Physiology Correspondent

ACCORDING to accepted theory the hormone responsible for initiating growth and moulting in the insect is secreted by the prothoracic glands when activated by the product of neurosecretory cells in the dorsum of the brain. The moulting hormone has been generally identified with the steroid ecdysone originally isolated by Butenandt and Karlson from developing pupae of *Bombyx*. But at present this theory is faced with certain problems. In the first place, the original ecdysone (α-ecdysone) is far less active in many insects than the more polar

A Ribosome's Muscle

ALTHOUGH the 50S and 30S subunits of *Escherichia coli* ribosomes have been reconstructed *in vitro* from appropriate mixtures of ribosomal proteins and RNAs, the function of most ribosomal proteins remains to be elucidated. Two exceptions are the L7 and L12 proteins of the 50S subunit which apparently function in translocation during protein synthesis. These two proteins are also remarkable because they differ in only one respect, the N terminal serine residue of protein L7 is acetylated whereas the N terminal serine of L12 has a free amino-group. In *Nature New Biology* next Wednesday (March 14) Wittman's group, Thammana *et al.*, report data which indicate that each 50S subunit contains at least two and probably three copies of L7 and/or L12.

Estimates of the amounts of L7 and L12 proteins that can be recovered from ribosomes labelled uniformly indicate that each ribosomal subunit has at least one copy of each protein. A quantitative immuno-precipitation procedure also indicates that each 70S ribosome contains approximately three L7/L12 molecules. In short, all the data Thammana *et al.* have obtained indicate that in the ribosomes isolated from bacteria growing at different growth rates the total amount of L7/L12 remains constant—three molecules per ribosome—even though the proportion of acetylated L7 molecules to unacetylated L12 molecules may vary.

Why do ribosomes contain multimeric copies of L7/L12 but only single copies of most other ribosomal proteins? Both L7/L12 have chemical similarities to contractile proteins which usually operate in multimeric assemblies. Thammana *et al.* suggest therefore that "the multiplicity of L7/L12 in the ribosome may reflect a requirement for a replete structure to affect movements of the ribosomal subunits with respect to each other".

hydroxy-derivative β-ecdysone, or ecdysterone. There is increasing evidence that ecdysone is converted by the insect into ecdysterone and that this is the active principle in moulting.

It has not proved possible, however, to extract either substance from the prothoracic glands of insects. Ecdysone can be extracted from adult *Bombyx*, in spite of the fact that the prothoracic glands break down completely before the adult emerges. In the eggs of *Bombyx* ecdysone reaches a high level before the prothoracic glands have developed (Ohnishi, Ohtaki and Fukuda, *Proc. Japan Acad.*, **47**, 413 ; 1971). Headless embryos of the locust *Schistocerca* undergo the two normal embryonic moults without the presence of the prothoracic gland (Miciarelli and Sbrenna). Moulting in *Rhodnius* can be prevented for several weeks if the haemocytes are put temporarily out of action by the injection of indian ink ; but if ecdysone is injected there is no delay. In the caterpillar of *Calpodes*, if the head is tied off and a ligature applied between the thorax and the abdomen, the thoracic fragment will duly moult if ecdysone is injected into it ; it will not moult if the prothoracic gland is implanted—unless a part of the abdomen is included in front of the ligature (Weir, *Nature*, **228**, 580 ; 1970).

The cytoplasmic changes that take place in the epidermis during wound healing are identical with those induced by ecdysone during moulting. These and other observations have led to the suspicion that the prothoracic glands do not secrete ecdysone (cf. Hoffmann and Joly, *CR Acad. Sci., Paris*, **257D**, 1665 ; 1972) but perhaps another hormone which induces ecdysone secretion by some other organ or tissue in the abdomen. Possible candidates are the haemocytes, fat body, pericardial cells, oenocytes, even the epidermal cells.

The other principal ecdysone problem is its site of action. Soon after the isolation of ecdysone in the early 1950s it was shown in *Rhodnius* that the earliest demonstrable effect of the hormone was the renewal of protein synthesis in those cells actively concerned in growth ; as evidenced by nucleolar enlargement, a great increase in nuclear and cytoplasmic RNA within an hour or two of its application, coupled with rapid multiplication of mitochondria. This was the first rational interpretation of the mode of action of a growth hormone and was soon adopted also for the growth hormone of vertebrates. But the site of action has remained obscure.

The observation made originally by Clever and Karlson (1960) that ecdysone alters the puffing pattern in the giant chromosomes of larval Diptera suggested a site very close to the genes themselves. In the tanning of the integument in blowfly larvae, which is a very sensitive test for ecdysone, the hormone induces the synthesis of the key enzyme DOPA-decarboxylase. Using inhibitors of RNA and protein synthesis, Sekeris (*Gen. Comp. Endocrinol., Suppl.* **3**, 149 ; 1972) shows that synthesis of the enzyme protein is dependent on newly synthesized RNA. Ecdysone stimulates the synthesis of nuclear RNA within 1 h after administration and acrylamide gel electrophoresis, and appropriate labelling show that qualitative differences in cytoplasmic RNA are induced by the hormone action. Very recently Emmerich (*Gen. Comp. Endocrinol.*, **19**, 543 ; 1972) has demonstrated the existence of receptor proteins for ecdysone in the cytoplasm of *Drosophila* salivary glands. Complexes between protein and ecdysone have been recognized also in the nucleus, where they are confined to the non-histone fraction of the chromatin. Purified chromatin from the glands will also bind ecdysone on incubation *in vitro*, but to a lesser extent than occurs *in vivo*.

PATHOGENIC BACTERIA

Phyto and Entomo

from our Soviet Correspondent

EXPERIMENTS carried out at the Institute of Microbiology and Virology of the Ukrainian Academy of Sciences indicate that certain bacteria can be pathogenic for both plants and insects (*Dopov. Akad. Nauk Ukr. RSR*, Ser. B (1), 80 ; 1973). Unlike previous studies which postulated a symbiotic or parasitic relationship between phytopathogenic bacteria and insect "hosts", this investigation demonstrates that the same strain of bacteria can be both phyto- and entomopathogenic.

Various strains of the bacterial genus *Erwinia* were isolated from infected beech, cucumber and cauliflower plants. Cabbage leaves were treated with a suspension of the bacteria of strength 1×10^5 ml.$^{-1}$ and the leaves were fed to Colorado beetle larvae.

On the fifteenth day following infec-

Selection for RNA Secondary Structure

ALTHOUGH the nucleotide sequences of only a few messenger RNAs have been analysed, it is quite clear that many messenger RNA molecules contain extensive regions of base-paired secondary structure. Such secondary structure may have a role in controlling the transcription and/or translation of the messengers. Because the presence of base-paired regions in a messenger RNA restricts the number of different amino-acids that can be coded by that messenger, it can be argued that during the evolution of some proteins, selection pressure has acted not only directly on the amino-acid sequence of the proteins but also on the RNA molecules themselves, so as to maintain some necessary secondary structure.

Is there any evidence for direct selection, during evolution, for messenger RNAs with particular secondary structures? Ball, who in *Nature New Biology* next Wednesday (March 14) reports an interesting analysis of the codons of the RNA bacteriophage MS2 coat protein cistron, believes that "the amino-acid sequence of MS2 coat protein has been subjected during its evolution to rearrangement in the interests of the secondary structure of the messenger RNA".

As Ball points out, there seem to be three possibilities controlling the relationship between an amino-acid sequence and the secondary structure of the messenger RNA that specifies that amino-acid sequence. First, selection pressure might act solely on the amino-acid sequence without regard to the secondary structure of the RNA. Second, selection might act not only on the amino-acid sequence but also on the choice between synonymous degenerate codons so as to maximize secondary structure of the RNA within the limits set by the amino-acid sequence. Third, selection pressure might act on the choice of synonymous and non-synonymous codons changing the amino-acid sequence in the interests of the secondary structure of the messenger RNA.

The great extent of base pairing of MS2 coat protein RNA seems to eliminate the first possibility. By classifying codons according to the number of base options (alanine codon $GC^{U\,C}_{A\,G}$ is classified as having base options 1,1,4) Ball has analysed the codons that occur in the base paired regions of MS2 co-protein RNA. He concludes that "there is no clear correlation between the degree of pairing and the number of base options indicating that the degenerate positions do not make an exceptional quantitative contribution to pairing".

If this is the case, as it seems to be, then one can only conclude that selection pressure has acted directly on the sequence and therefore secondary structure of this particular mRNA. In other words, the amino-acid sequence may have evolved in the interests of the secondary structure of the RNA molecule. Whether such selection is widespread remains to be seen, for it always has to be remembered that MS2 RNA has to be encapsidated in a virus particle and may therefore have been subjected to selection pressures not exerted on cellular messengers.

tion, mortality among the larvae infected with certain strains of phytopathogenic bacteria was significantly higher than among the control larvae which had been fed non-infected leaves. The highest mortality rates were observed for *Erwinia* sp. 418_3 and 449_2 isolated from beech and for *E. aroideae* 144 isolated from cauliflower (53.3 ± 6.7 per cent, 58.5 ± 1.6 per cent and 40.2 ± 2.6 per cent respectively, as against 20.4 ± 11.3 per cent among the control larvae). By day 20, mortality from *Erwinia* sp. 418_3 was 93.3 ± 6.7 per cent as against a control value of 23.8 ± 11.1 per cent. Significant increases were also observed for *Erwinia* sp. 262_{2a} and 521_{3a} from beech (81.3 ± 6.3 per cent and 74.6 ± 5.1 per cent respectively after 26 days, control value 46.6 ± 9.7 per cent). Other strains of *Erwinia* from beech and cauliflower and strains obtained from cucumbers produced no statistically-significant increase in mortality.

After 26 days imago formation took place among the surviving larvae, and further development proceeded normally. The number of eggs laid by the adult beetles varied considerably but seemed unrelated to the type of infection. The authors conclude that the entomopathogenic properties of phytopathogenic bacteria depend on the bacterial strain and its natural habitat. It is noteworthy that anaerobic strains in general had a greater effect on the larvae, irrespective of their origin.

In a converse series of experiments, entomopathogenic bacteria were isolated from the haemolymph of sugarbeet weevil larvae, and identified as being of types close to the phytopathogenic *E. caratovora* and *E. aroideae*. These were found to produce disease in onion seedlings and unripe tomato fruits, with symptoms similar to those from typical phytopathogenic strains. The *E. aroideae* analogue seemed more virulent than that of *E. caratovora*.

It seems therefore that in natural conditions certain plants and insects may be susceptible to the same pathogenic bacteria — a fact which, the researchers stress, should be taken into account in any attempt to develop microbiological methods of combating crop pests and diseases.

BREAST CANCER

Anti-oestrogen Therapy

from a Correspondent

ADMINISTRATION of sex hormones or their analogues, whether androgenic, oestrogenic or progestogenic, can produce temporary remission in about one-quarter to one-third of patients with advanced breast cancer. Preparations of anti-oestrogens have also been used, for example, ethamoxytrithetol ('MER-25'), triparanol and clomiphene citrate,

three compounds which are analogues of the non-steroidal oestrogen chlorotrianisene (chlorotris (p-methoxyphenyl) ethylene). The number of patients treated by these compounds, however, has been too small for any conclusion to be drawn about their usefulness.

There have, however, been trials recently in women with advanced breast cancer of a new anti-oestrogen, 'Tamoxifen' (ICI, 46,474), which is related chemically to clomiphene. Cole *et al.* (*Brit. J. Cancer*, **25**, 270 ; 1971) used doses of 10 to 20 mg daily in patients who had already been treated by a variety of means. Ten of the forty-six patients treated had a good response as judged by reduction in size of the soft tissue masses and/or radiological evidence of regression of pulmonary or bone metastases and a further seventeen patients had a partial response. The response rate was similar to that seen with other forms of hormone treatment. Side-effects were mild; only two patients stopped treatment because of them.

Better results have now been reported by Ward (*Brit. Med. J.*, **1**, 13 ; 1973) in a study of sixty-eight patients with advanced breast cancer. Sixty per cent of the patients receiving daily doses of 20 mg of 'Tamoxifen' and 51 per cent of those receiving 10 mg each day achieved some reduction in the size of the tumour and in 38 per cent of the women this reduction was to one-half or less. Breast tissue and breast tumours contain "receptor" proteins which take up and bind oestrogens and it is possible that 'Tamoxifen' acts by preventing the uptake of oestrogens.

VIRUSES

The RSV Genome

from our Cell Biology Correspondent

ROUS sarcoma virus was discovered in 1911 by Peyton Rous and if anybody could raise the energy to compile a complete bibliography of reports of work involving this virus they would surely end up with a massive tome which might well continue growing exponentially for some time to come. But in spite of the vast effort that has been spent and the vast literature that has accumulated the size and structure of the RNA genome in RSV particles are still not known for certain.

The problem is that none of the RNA molecules that can be extracted from the virions is reproducibly infectious, so although the 60–70S RNA in these particles probably is or includes the viral genome this has never been proven unequivocally. This 60–70S RNA (and let us assume it includes the viral genome because the properties of the 4S, 7S and other minor RNAs that can be extracted from RSV particles strongly suggest that they cannot be genomic) has curious properties. Most notably on denaturation, either by heating or treatment with denaturants such as DMSO, it sediments at 30–35S instead of 60–70S. Moreover, the 30–35S RNA has a greater electrophoretic mobility than has the 60–70S RNA. Clearly these differences can be explained in two ways ; either the 60–70S RNA is a single polynucleotide chain which can undergo dramatic

Double Helix from Mononucleotides and Polymer

IT has not so far been evident that double-helical structures are formed when mononucleotides associate with a single-stranded polynucleotide. For the system of adenine with polyuridylic acid the evidence is that only triple-stranded helices, with a base ratio of 2U:1A, are formed. Now Pörschke, Hoffman and Senear, writing in next Wednesday's *Nature New Biology* (March 14), have found that a two-stranded complex, just like poly (A) · poly (U), can in fact be formed when an adenine derivative stacks onto poly (U). In N-6,9-dimethyladenine the additional hydrogen bonding site required for the attachment of a second poly (U) strand is blocked. The dimethyladenine also has a strong stacking propensity, and binds readily to poly (U).

Miles and his associates have already shown that the infrared spectrum of the complex is similar to that of poly (A) · poly (U). The first demonstration that Pörschke *et al.* give of 1:1 stoichiometry is by equilibrium dialysis, in

which the binding ratio is incompatible with saturation at one dimethyladenine to two uracil residues. Second, a spectrophotometric continuous-variation mixing experiment gives a sharp maximum of hypochromicity at a base ratio of 1:1. The binding is cooperative and the complex displays a sharp melting curve like a two-stranded polymer.

That base pairing with hydrogen bonding is indeed involved was confirmed by showing that 6-N,N' dimethyladenine, in which both hydrogen atoms at position 6 are replaced, does not form a complex with the poly (U). By the temperature jump method, the kinetics of the interaction of the monomer with poly (U) were found to be characterized by a relaxation time in the μs range, which is about three orders of magnitude slower than triple-strand interactions, in which there are three reactants. The stacking of monomers alone, in the absence of base pairing, occurs at a rate which is some three orders of magnitude faster again.

changes in conformation, or the 60–70S RNA comprises an assembly of 30–35S subunits held together by heat labile, DMSO labile bonds—in short, hydrogen bonds. If the second model is correct, as is widely believed, and if relationships between sedimentation coefficients and molecular weight derived for small RNA molecules are valid it is simple to calculate that the 60–70S RNA has a molecular of weight about $10–12 \times 10^6$ and that the putative 30–35S RNA subunits have a molecular weight of about $3.3–3.5 \times 10^6$.

Two lines of evidence support the notion that the 60–70S RNA of RSV is an aggregate of subunits—in other words that the RSV genome is segmented; first, when chick fibroblasts are infected by two different strains of RSV recombinant virus particles form a considerable proportion of the progeny. This high frequency of recombination, which is also a characteristic of influenza virus—a virus with a single segmented RNA genome—can readily be explained if the RSV genome comprises three or four RNA chains, for in mixed infections progeny virions may assemble by taking combinations of RNA subunits of the two parental types. Second, Cheung et al. (1972) and Canaani et al. (1973) have just reported quite different physicochemical evidence which suggests that 30–35S RNA may be a precursor of 60–70S RNA.

Cheung et al. (Virology, **58**, 51 ; 1972) harvested Prague strain RSV from chick fibroblasts at 5, 10, 20, 60 and 180 min and 12 h and 24 h intervals. The 5 min harvest virus proved to contain little 68S RNA, but it contained a heterogenous RNA with a median sedimentation coefficient of 55–60S which on denaturation yielded 36S RNA and RNA sedimenting between 36S and 4S. By contrast 24 h harvest virus particles yielded a homogenous 68S RNA which denatured to yield homogenous 36S and 4S RNAs. Particles harvested at intermediate times yielded RNA patterns which were intermediate between these two extremes.

Canaani et al. (Proc. US Nat. Acad. Sci., **70**, 401 ; 1973), who found themselves down wind, so to speak, of Cheung and his colleagues, made similar experiments harvesting Prague RSV particles at only 3 min intervals. They then compared the sedimentation properties and electrophoretic mobilities of the RNA in 3 min harvest virus with the RNAs of virus harvested at hourly intervals. They found the rapidly harvested virus contains a little 60–70S RNA but a large amount of 30–4S RNA and a variable amount of 4–12S RNA. Furthermore, incubation at 40° C for 3 min of the 3 min harvest virus results in the conversion of most of the 30–40S RNA into 60–70S RNA.

These results suggest that 30–4S RNA is a precursor to 60–70S RNA and, as Canaani et al. point out, the conversion may involve the association of 4S RNA. They say this for two reasons ; first, when 60–70S RNA is denatured back to 30–40S RNA five times more 4S RNA is released than is released when 30–40S RNA from 3 min virus is denatured directly ; second, 30–40S RNA from 3 min virus is about five-fold less efficient as a template for reverse transcriptase than 60–70S RNA, and 4S RNA is believed to act as a primer for reverse transcription. Of course, the report (Jarrett et al., 1971) that some free 30–40S RNA can be isolated directly from feline leukaemia virus particles harvested at long intervals gains significance in the light of these experiments.

CEPHALOPODA

Deep-sea Cirromorphs

DEEP-SEA cirromorphs (Cephalopda) have been recorded and photographed for the first time in the Arctic Ocean (Pearcy and Beal, Deep-sea Res., **20**, 107 ; 1973). Out of more than 2,900
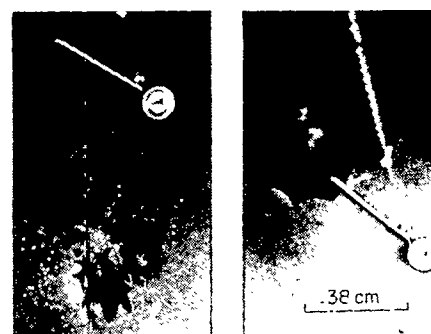
photographs taken off Point Barrow, Alaska, from USS Staten Island, cirromorphs appeared in twenty-one, representing a maximum of twelve individuals ; all were at depths ranging from 3,219 to 3,786 m.

The cirromorph in these photographs (taken 15 s apart) is swimming upright or perpendicular to the bottom, with its fins appearing to stroke horizontally. The arms and web in this sequence are first joined together and extend toward the bottom (left) and then expand laterally to form a large umbrella-like surface (right). A second mode of locomotion—swimming in the horizontal position, which is more typical of cephalopods—was also noted.

Initiation of Eukaryotic Protein Synthesis

NEXT week, in Nature New Biology (March 14), Schreier and Staehelin present a detailed study of the roles of two purified protein factors involved in polypeptide chain initiation in eukaryotes. These authors suggest that the mRNA-independent binding of the initiator Met-RNA$_f$ to the 40S subunit is the first step in polypeptide chain initiation in eukaryotes and that this complex then directs the building of mRNA.

Four initiation factors, IFE$_{1,2,3,4}$, were purified from rabbit reticulocytes by means of DEAE-cellulose followed by preparative glycerol density gradients. IFE$_2$, IFE$_3$ and GTP are absolutely required for the binding of Met-RNA$_f$ to 40S subunits in the absence of mRNA. Two forms of IFE$_3$ with sedimentation coefficients of 15S and 17S were detected, the smaller form probably being a degradative product of the larger.

With initiator Met-RNA$_f$ purified IFE$_2$ but not IFE$_3$ formed a complex which was GTP-dependent but ribosome and template-independent. In the presence of artificial template poly (A,U,G) and GTP, IFE$_3$ alone did not promote formation of the [40S Met-tRNA$_f$] initiation complex, whereas IFE$_2$ did. When natural globin mRNA replaced the artificial template, IFE$_2$ no longer promoted binding of Met-tRNA$_f$ and 40S subunits, but on the addition of IFE$_3$ to IFE$_2$ the complex was formed. Thus

IFE$_3$ is required for binding of natural mRNA. Complex formation in the presence of IFE$_2$ and IFE$_3$ was just as efficient when mRNA was omitted. Thus IFE$_3$ promotes template-independent binding of Met-tRNA$_f$ (presumably complexed with IFE$_2$ and GTP) to 40S subunits.

The [Met-tRNA$_f$ 40S] complex sedimented very close to the original 40S subunits. But in the presence of excess IFE$_3$, subunits which had not bound Met-tRNA$_f$ sedimented at about 48S, a sedimentation rate compatible with a particle composed of a 40S subunit complexed with IFE$_3$. Schreier and Staehelin suggest that IFE$_3$ combines initially with a 40S subunit to direct the binding of Met-tRNA$_f$. Subsequently the bulk of IFE$_3$ must dissociate from the initiation complex but a component of it may remain attached, to direct binding of mRNA. If IFE$_3$ were heterogeneous with regard to such a component, this might provide a mechanism for mRNA selection.

In conclusion, IFE$_3$ promotes the mRNA-independent binding of Met-tRNA$_f$ to the 40S ribosome subunit in the presence of IFE$_2$. In that the initiator tRNA is bound first to the ribosome and helps the binding and correct phasing of messenger rather than the converse, this model of polypeptide chain initiation in eukaryotes is fundamentally different from the bacterial mechanism.

MUSCLE

Regulating the Scallop

from our Molecular Biology Correspondent

ONE of the most interesting developments in muscle biochemistry in recent years is the partial resolution of the regulatory machinery, which enables the myosin ATPase to respond to small changes in the concentration of calcium supplied by the sarcoplasmic reticulum. In the mammalian systems, on which most of the work until just now has been done, the site of regulation is in the thin filaments, the effect of the calcium, which binds to one of the troponin subunits, being transmitted by way of the other troponin components and tropomyosin to the actin. This causes a change in the affinity of the actin for the myosin heads, reaching out towards it from the thick filaments. Szent-Györgyi and his colleagues have been looking at the muscles of more primitive creatures, and here it seems that regulation is encompassed in a totally different manner, and operates not at the thin filaments but rather the myosin heads. Szent-Györgyi, Szentkiralyi and Kendrick-Jones (*J. Mol. Biol.*, **74**, 179 ; 1973) now unfold a remarkable story concerning the mechanism of regulation of scallop muscle.

Fortune has to an extent favoured them, for the wily scallop has incorporated a regulatory subunit into its myosin, which, unlike the minor chains of numerous other myosins that have been looked at, can be removed without reducing the protein to an enzymatically inert porridge. The myosin extracted from scallop muscle is superficially indistinguishable from that of mammals: its hydrodynamic and optical rotatory properties are the same, and so is its length in the electron microscope, as well as the segment long spacing in fibres. When exposed to proteases under the right conditions it gives rise to enzymatically active soluble fragments, corresponding to heavy meromyosin and sub-fragment-1 (or isolated heads). Also like rabbit myosin, it contains light chains, which in SDS-gel electrophoresis come out at a molecular weight of about 18,000, and in a ratio of three chains per myosin molecule.

There are, it turns out, two types of light chain in the scallop, one of which contains cysteine and is present in a ratio of two copies per myosin. The other, of which there is only one copy per myosin molecule, is dissociated when EDTA is added to sequester divalent metal ions. It is this molecule which is the "regulatory subunit", in that it confers calcium response on the myosin. Thus, the ATPase activity is unaffected by the addition of calcium ions when the critical light chain has been stripped off, whereas the ATPase of intact myosin

with its complement of light chains is strongly inhibited by removal of calcium. When the preparation of light chains is added back to the stripped myosin, the calcium sensitivity is restored. The stripped myosin still binds calcium, but binding plots indicate that probably one site has been lost. The light chain is not of itself, however, capable of taking up calcium. The other (cysteine-containing) light chains remain firmly stuck to the myosin, and their removal by more drastic methods leads to irreversible denaturation.

The independence of the thick and thin filament-dependent regulation mechanisms is spectacularly demonstrated by the interaction of the desensitized scallop myosin, denuded of its regulatory light chain, with the rabbit actin-tropomyosin-troponin system, with which it combines just like rabbit myosin to give a fully calcium-regulated actomyosin. This points again to the evolutionary stability of actin compared with myosin, at which evolutionary pressures are evidently mainly directed. Rabbit myosin will induce a high and calcium-independent ATPase activity in a mixture of actin with excess scallop myosin. It seems therefore that when there are no calcium ions about, the scallop myosin does not combine with actin, so that the actin filaments are available for reaction with a competing species. Neither, in consequence, is the ATPase of the scallop myosin stimulated by actin in the absence of calcium. Like the regulatory protein system of mammalian thin filaments, then, the sensitizing subunit of the scallop myosin blocks the interaction with actin. The oddest aspect of this engrossing story is the stoichiometry. In principle it is possible, with the aid of some allosteric hand-waving, to explain the calcium response of a system bearing a regulatory subunit on only one myosin head. The authors eschew such intellectual contor-

tions, and postulate instead that the regulatory chain physically links the two heads, and functions only when so located. In support of this kind of scheme is the finding that active isolated heads (8–1) from the scallop myosin contain the regulatory light chain, but have no calcium sensitivity.

A curious twist to the picture of regulation in mammalian muscle emerges from an observation by Bailin and Bárány (*J. Biol. Chem.*, **248**, 373 ; 1973), who find that rabbit myosin, dinitrophenylated to the extent of 1.5 modifying groups per molecule, displays no calcium sensitivity in its complexes with actin, tropomyosin and troponin. Partial removal of the dinitrophenyl groups leads to reappearance of calcium sensitivity. This seems to indicate that the myosin when modified no longer recognizes the difference between the inhibiting and non-inhibiting states of the thin filaments.

SOLAR SYSTEM

Primordial Field

from our Geomagnetism Correspondent

THE strength of the interplanetary magnetic field is now of the order of tens of gammas. But has it always been so? And in particular, was it quite so low at the time of the origin of the Solar System? In the absence of any other information, it is often taken as axiomatic that the interplanetary field has always been negligible ; but Sonnet *et al.* (*Astrophys. Space Sci.*, **7**, 446 ; 1970) have postulated otherwise, and primordial magnetic fields of the order of 1 oersted ($10^5\gamma$) are apparently required by the cosmological theories of Fowler *et al.* (*Geophys. J.*, **6**, 148 ; 1962).

In principle, it should be possible to determine the intensity of the primordial interplanetary field from carbonaceous chondritic meteorites, for Banerjee and

Drag Reduction for a Rotating Disk

ALTHOUGH drag reduction in turbulently flowing liquids containing small amounts of polymers like polyacrylamide is fairly well investigated, both practically and theoretically, it is the possibility of drag reduction under conditions of laminar flow that is in many ways of particular interest. For one thing laminar flow is more commonly encountered than turbulent flow.

In next Monday's *Nature Physical Science* (March 12) Kale, Mashelkar and Ulbrecht show that drag can be reduced when a disk rotates under laminar conditions in an appropriate polymer solution. What they have done is to investigate the relationship between torque and angular velocity for disks between 7.5 and 15 cm in diameter in solutions

of carboxy methyl cellulose—an inelastic fluid—and in three solutions of polyacrylamide of varying strength. It turns out that for a given angular velocity (plotted by Kale *et al.* as a moment coefficient) the torque is significantly reduced in the case of the polyacrylamide solutions.

Kale and his colleagues draw attention to the fact that others have shown drag reduction in laminar flow to be possible in situations like flow in a curved tube and flow round a sphere, but they place their own work firmly on a practical footing when they say that "for centrifugal pumps with enclosed disk-type impellers there is likely to be a better pumpability with viscoelastic liquids".

Hargraves (*Earth Planet. Sci. Lett.*, **10**, 392; 1971) recently showed that some such chondrites contain a moderately strong and stable natural remanent magnetization (NRM). In this branch of geophysics, of course, the gap between principle and practice can be quite wide, as the difficulties in obtaining palaeointensities from even very young terrestrial rocks prove. Nevertheless, both Banerjee and Hargraves (*Earth Planet. Sci. Lett.*, **17**, 110; 1972) and Butler (*Earth Planet. Sci. Lett.*, **17**, 120; 1972) have independently succeeded in determining at least minimum intensities of the primordial field and find them to be several orders of magnitude higher than commonly supposed.

Banerjee and Hargraves have used the Orgueil, Murchison and Allende meteorites which are carbonaceous chondrites representative of Wiik's (*Geochim. Cosmochim. Acta*, **9**, 279; 1956) Types I, II and III respectively. The principal field determination was carried out using a modified form of the Thellier method (backed up by thermomagnetic, opaque mineralogy and electron probe microanalysis studies) to assess stability and identify the magnetic carriers. The Allende chondrites proved to be the most stable magnetically (thus giving the most reliable data), the magnetic carriers being very fine single-domain grains, probably of NiFe. Even so, only temperatures up to 135° C could be used for the intensity determination because of thermally-induced chemical changes at higher temperature. The result of four determinations on two samples was an average palaeointensity of 1.09 oersted. The Murchison and Orgueil chondrites were relatively less stable, the usable temperature ranges being lower. Average palaeointensity values from these were 0.18 oersted and 0.67 oersted, respectively.

Butler has concentrated solely on the Allende meteorite and finds an average ancient field strength of 1.1 oersted. In a situation fraught with so many practical problems, such agreement is startling and, as Banerjee and Hargraves admit, must be regarded as fortuitous. The order of magnitude agreement is, however, important. Moreover, there are other reasons for regarding exact values with some caution. For example, the intensity determination methods used are based on the assumption that the NRM of the samples is TRM (thermoremanent magnetization). In the case of the Allende, chondrite there is convincing evidence that this assumption is warranted, although in the other examples the validity is less secure. The point to bear in mind here is that TRM is the most effective magnetization process, so that if other processes were responsible for the magnetization the obtained palaeointensities would be underestimates. In other words, the

values derived by Banerjee and Hargraves and Butler are at least minimum values.

Because there is no evidence to suggest that the Allende chondrite has been reheated since its formation (indeed, there is evidence to the contrary), the conclusion must be that magnetization took place in a field at least 10^4 times higher than the present interplanetary field and of the order of magnitude of the present terrestrial surface field. This presumably refers to 4.44×10^9 yr ago, the potassium-argon age of the chondrules in the Allende meteorite. As Butler points out, however, alternative interpretations are possible. The strength of about 1 oersted only applies to the ancient interplanetary field if the Allende was actually magnetized in that field. It could, of course, have acquired its magnetization in the field of its parent body. In this case, the parent planet would have required an extremely high magnetic moment at a very early stage in the formation of the Solar System.

SEMICONDUCTORS

What is New?

from a Correspondent

THE opportunity for asking this question was afforded by the celebrations in connexion with the twenty-fifth anniversary of the transistor and, in particular, in a symposium held by the Institution of Electrical Engineers in London on February 14. A small exhibition of the

development of the transistor is open at IEE headquarters and is worthy of a visit.

The symposium did not forget the social aspects of the invention of the transistor, which were reviewed by Professor W. E. Farvis (University of Edinburgh); but the technical contributions and the lively discussion which followed concentrated rather on the question of the next step in the field of electronic devices. The five invited speakers were all members of research laboratories attached to leading British semiconductor manufacturers and they were all clearly adept at presenting the potential profitability of their ideas for new developments to their financial managers. They thus had an interest in presenting at least an appearance of hard-headedness. Although this rather limited the distance of the look forward and inhibited the range of an otherwise lively discussion, it allowed a firm and highly informal contemplation of the next stages in silicon technology.

The first talk was perhaps an exception to this generalization. Dr J. Evans (Standard Telecommunications Laboratories) talked about new materials and the new electronic functions which they might perform in the future. He began with an account of the versatility of gallium arsenide, which was at first used as a material for bipolar transistors but has now unexpectedly found application in light-emitting devices and as a microwave oscillator and a field-effect transistor. He held this up as an example of how to pick new materials

Soft X-ray Structure of Cassiopeia A

OBSERVATIONS of Cas A from Copernicus are reported in next Monday's *Nature Physical Science* (March 12) by Fabian, Zarnecki and Culhane. The diagram shows an X-ray contour map of the source in the energy range 1.4 to 4.2 keV, superimposed on the Uhuru error box for the source 2U2321 + 59. Clearly, the two objects are the same, as was already suspected.

The detail shown in the contour map is reminiscent of the first radio contour maps obtained of this source, and the overall distribution of X-rays is best explained by an annular source of outer diameter 5.5 ± 1.5 arc min and inner diameter 2.0 ± 2.0 arc min—this is definitely not a compact source of X-rays, even though it might have been expected that a collapsed object would have been left at the centre of this supernova remnant, which is only about 300 years old. "The data are suggestive", say Fabian *et al.*, "of a shell source" in which X-ray generation occurs either through thermal bremsstrahlung from a blast wave or through the synchrotron process.

Much remains to be discovered from

further detailed studies of the source; it is particularly interesting to compare the present X-ray observations with early radio maps of Cas A and with the best detailed map now available, made at 2.7 GHz, which the MSSL team reproduce in their article. If the accuracy of X-ray astronomy proceeds at the present pace, it may not be long before comparable high resolution X-ray maps of Cas A and other extended objects are available.
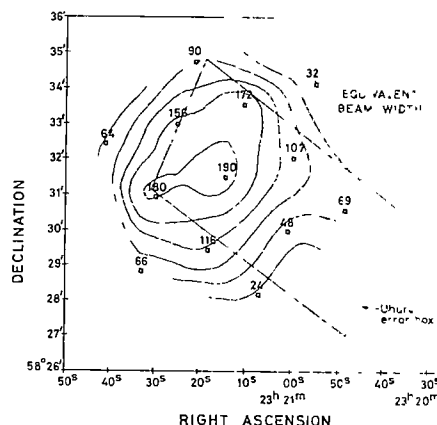
for research. Choose one with versatility, he said, because, even if it does not satisfy the original requirement, several other unexpected uses are likely to emerge. On this principle, STL has just announced an extensive commitment to research in glasses, which may be useful as detectors, switches, memories, light guides and in about twenty other ways listed by the speaker. Dr Evans listed several electronic functions (lasers, surface acoustic wave transducers and so on) which should find important new applications in the future.

Dr D. H. Roberts (Plessey, Allen Clark Research Centre) confined his attention to the "third generation" of transistor devices—silicon bipolar integrated circuits. He left out metal-oxide-semiconductor (MOS) integrated circuits on the grounds that they are difficult to control—although this implied deficiency did not go undefended in the discussions. He examined the new techniques of making arrays of very small transistors and envisaged a single bipolar device smaller than 1,000 μm^2. The first commercial transistors were more than 1,000 times larger. Dr Roberts rightly termed knowledge of the physics of diffusion and other silicon processing techniques as "pathetic", and appealed for more work in that field.

Two subsequent speakers performed similar tasks of presenting the problems and plans for packing more logic functions into a single slice of silicon (an art called "large-scale integration"). One wants to get 5,000 logic gates on a silicon chip with dimensions no larger than 1 cm. Mr R. A. Hilbourne (Mullard, Southampton) dealt chiefly with computational logic circuits and Mr W. Holt (Plessey, Allen Clark Research Centre) dealt with semiconductor memories. Mr Hilbourne stressed that circuit design techniques, rather than new material technology, hold the key to this art but thinks that it is difficult to decide who should do the design—the user or the chip manufacturer. Hewlett-Packard, for example, left the detailed chip layout for their pocket calculator in the hands of the chip supplier but carried out a parallel computer simulation study of their own. The aid of the computer in layout and testing is absolutely essential. Even with completely computerized testing, Mr Hilbourne was worried about the "escape limit"—the areas of integrated chip which, for reasons of time, could not be tested, even by an ultra-fast computer checkout, before the chip was packaged and sent to the customer. Mr Holt's account was principally of the internal battle waged between various semiconductor approaches and the external battle between semiconductors and other memory techniques such as magnetic cores, magnetic bubble

domains, plated wires, tapes and cards. The market is great, the memory requirements are varied and so are the technological approaches. This leads to the "memory-of-the-month-effect", he said, a confusion and flux of fortunes which must be a manufacturer's nightmare. Nonetheless, Mr Holt guided the symposium through the relative merits of bipolar transistors, MOS in several forms and metal-nitride-oxide-semiconductor (MNOS) devices with clarity. One can, however, expect 10^8 years of stable data storage, even from the volatile-looking MNOS system.

Dr D. Burt (GEC, Hirst Research Centre) closed the technical session with an account of the work of the centre on the charge-coupled device (CCD)—an offshoot of MOS technology. His clear account of the principles made it easy to follow the various approaches GEC has made to dynamic storage of information and to imaging. GEC expected trouble in producing gaps between electrodes of 2 μm for great total elec-

trode lengths (100 cm on a large chip). Trouble was not encountered in the laboratory but Dr Burt wondered how this process would fare in production. The trouble with the device principle is that one is juggling with data bits represented by a few pC of charge (only 10 million electrons). Surface states could suck these up and delay the necessary crisp transfer along the chain of "potential wells" in the semiconductor. GEC is managing transfer efficiencies of 99.5 per cent and Bell Telephone Laboratories claims 99.8 per cent.

Perhaps here, in the tail of the symposium, was the most forcible riposte to the earlier statements that process control in the MOS device system is too difficult for its wide competitive success over Shockley's bipolar transistor in the future. Not only may the MOS logic circuit make inroads into the bipolar market but its offshoot, the CCD array, may also replace television camera tubes in due course.

Circular Polarization in Compact Radio Sources

THE first observational investigation of the frequency dependence of circular polarization of compact radio sources is reported in next Monday's *Nature Physical Science* (March 12). Although the existence of such polarization in some sources has been known for two or three years, the measurement of the very low levels of polarization requires very careful measurements. Simultaneous observations to determine frequency dependence of the polarization require, in addition, collaboration by teams operating different antennas at widely separated points on the Earth. So these observations are something of a landmark in the history of radio astronomy.

The antennas used were the 140-foot at the National Radio Astronomy Observatory (NRAO), the NRAO interferometer and the 150-foot at Algonquin (ARO). These provided simultaneous measurements at 1,666 MHz, 2,695 MHz, 8,085 MHz and 13,500 MHz. In addition, some data obtained at different times with the ARO instrument may usefully be incorporated in the study, which was undertaken by Seaquist, Gregory, Biraud and Clarke. The three sources studied are 3C 138, 3C 279 and BL Lac. Each of them is circularly polarized at 1,666 MHz, but only 3C 138 shows marginal evidence for such polarization, at the 2 sigma level, at the higher frequencies.

By utilizing data obtained at other epochs, Seaquist *et al.* conclude that the degree of circular polarization for 3C 279 is small at both low and high frequencies and large at intermediate frequencies (see diagram), with a maximum

around 3,000 MHz. This suggests that one of the four synchrotron-emitting components believed to make up this source is much more strongly polarized than the other three. 3C 138 also shows evidence of variation of degree of circular polarization with frequency.
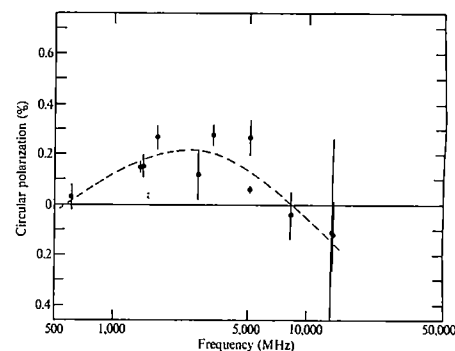
But perhaps most interest in this work will be focused on BL Lac. The measurements provide a new test by which the properties of this object can be compared with those of QSOs; unfortunately BL Lac is rapidly variable in circular polarization, which makes it useless to combine data from different epochs. Taken alone the November 1972 data indicate polarization at 1,666 MHz and hint at polarization at 2,695 MHz. But even these observations must be regarded as dubious now that BL Lac has been found to vary strongly over time-scales of a few hours (Weistrop, *Nature Physical Science*, **241**, 157; 1973: see also *Nature*, **241**, 502; 1973). Really useful information about the circular polarization of BL Lac must, it seems, await another quantum jump in observing technique.

The Loch of Strathbeg

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The British Gas Corporation and Total Oil Marine have applied for outline planning permission to build a reception and transmission plant for North Sea gas on the disused airfield at Crimond in Aberdeenshire. This could have a considerable effect on the Loch of Strathbeg, Britain's largest coastal dune lake, which lies alongside the airfield, particularly because the proposed access for pipelines crosses both loch and dunes. This article describes why the loch is of particular interest.

THE Loch of Strathbeg in north-east Aberdeenshire, the largest coastal dune lake in Britain, is a lagoon approximately 3 km long, a little less than 1 km wide, 220 ha in area and 1 to 2 m deep, which was formed when a sand bar blocked the entrance to the ancient port of Rattray at the beginning of the eighteenth century[1-3]. Its water level fluctuated markedly at first, but was stabilized when a new outlet was cut in an unsuccessful attempt at drainage at the start of the period of agricultural "improvement" when the surrounding estates were put in order and planted with trees at the end of that century. The whole area has remained comparatively undisturbed since that time, apart from temporary use of the loch as a base for seaplanes during the First World War, and the establishment of an airfield at Crimond overlooking it from the west during the Second World War, when it was filled with moored logs to prevent hostile seaplanes from landing. Because the loch is now the best representative of its kind in Britain in terms of extent and freedom from alteration and pollution, is an important staging post for migratory waterfowl, and lies in the centre of an area which now seems likely to become increasingly industrialized, it seems timely to summarize the information available about it.

Geomorphology

The evolution of the area has been studied by Walton[4]. The underlying rock is gneiss, with occasional granite and quartzite outcrops, and slopes gently to the east. It is overlain by glacial deposits inland, but appears as a series of low headlands projecting through the dunes along the coast. It seems that during the last glaciation this corner of Aberdeenshire may have escaped the ice, and a series of indistinct raised shorelines inland may date from the last interglacial period (Fig. 1). The loch site may then have been eroded when the sea retreated during the glaciation by the streams now entering its inner extremities, perhaps swollen by melt water from the ice inland. In the immediate postglacial period the sea then rose again to cut another very distinct shoreline about 15 foot above the present one, and a series of shingle spits were progressively formed, extending south across the mouth of the resulting inlet, which was eventually closed by sand blowing up the coast from the south since the sea level returned to its present level about 5,000 yr ago. During the terminal stages of this process in the seventeenth century the harbour mouth at the south end became blocked. Rows of dunes extended north from Rattray Head, with a shallow inlet parallel to the coast. The lows of this inlet and the old channel now form dune slacks.

Limnology

The associated dunes are calciferous, and the loch is a moderately eutrophic water body with an alkalinity of 70 to 80 p.p.m. as $CaCO_3$ and a distinct saline influence now due to spray blown from the sea. As the loch is extremely shallow for its size the sandy bottom is brought into suspension during periods of high winds rendering the water turbid. Wave action has reduced much of the shoreline to wave-washed sand and gravel with only a limited amount of marginal vegetation, but in the more sheltered western arm there are some extensive beds of *Phragmites* with smaller patches elsewhere. Submerged vegetation, which forms one of the chief sources of food for wildfowl, is, however, plentiful, including *Chara aspera, Potamogeton filiformis* and *Littorella uniflora* in shallow water, with *Potamogeton pectinatus, P. perfoliatus* and *Cladophora* in deeper water. This plant assemblage is very characteristic of sandy eutrophic and particularly maritime lochs in Scotland.

The varied invertebrate fauna of the loch contains several species associated with very slightly brackish conditions, which occur rather infrequently in British lakes. The gastropod *Potamopyrgus jenkinsi* is extremely abundant and the amphipod *Gammarus duebeni* and the corixid *Sigara selecta* plentiful. The other invertebrates recorded are either species characteristic of a sandy substrate (for example *Caenis moesta, Arctocorisa germari* and *Sigara dorsalis*), wave-washed shores (for example *Tinodes waeneri* and *Oreodytes rivalis*) or weed beds in eutrophic conditions (for example *Cloeon simile,* Leptoceridae, *Sigara falleni* and *Callicorixa praeusta*). The zooplankton consists chiefly of the common association of *Daphnia hyalina, Cyclops strenuus* and *Diaptomus gracilis*. The abundance of invertebrates, particularly gastropods, forms a rich source of food for the trout, three-spined sticklebacks, flounders and eels, which are the only fish, and for some of the wildfowl.

Botany

The unusual geomorphological history of the area has resulted in the creation of a diversity of habitats of outstanding botanical interest. In addition to the loch and its

— Interglacial (50 foot) shoreline
---- Early post-glacial (15 foot) shore
— Modern shore
⬚ Raised shingle ridges
⬚ Dune systems
ᖫ Rock outcrops at Rattray Head
● Ruins of St. Marys Chapel at the site of the Royal Burgh of Rattray
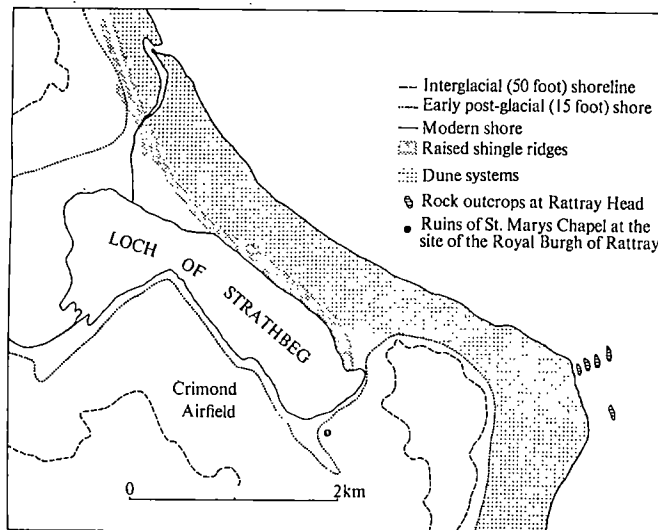
Fig. 1 The Loch of Strathbeg.

margins these comprise marshland, *Salix* scrub, salt marsh, dune slacks, and dunes built of sand containing a relatively high proportion of shell fragments. More than seventy species of vascular plants have been recorded within the boundary of the Site of Special Scientific Interest. These include one extremely localized species, *Ranunculus reptans*, which is confined to about five stations in the British Isles, several predominantly northern species, notably *Ligusticum scoticum*, here behaving rather atypically as a dune plant, and a few principally southern species of restricted distribution in north-east Scotland such as *Epilobium hirsutum*. This alone indicates that the locality is of special ecological significance.

In addition to the aquatic macrophytes already mentioned, attention may be drawn to the zonation of plant communities around the southern margin of the loch. Bordering on the dunes or fields is a zone dominated by *Phalaris arundinacea*, which includes such species as *Iris pseudacorus*, *Achillea ptarmica*, and *Myosotis scorpioides*. Nearer the loch, especially in the bays, this gives place to an *Eleocharis*

palustris zone, the upper part of which contains *Juncus articulatus*, *Leontodon autumnalis*, *Polygonum amphibium*, *Senecio aquaticus*, *Lotus uliginosus* and others. The lower part, around the edge of the water, is characterized by such species as *Carex nigra*, *Littorella uniflora*, *Myriophyllum alterniflorum*, *Equisetum fluviatile* and, where the cover is incomplete and most species are dwarf or decumbent, *Ranunculus reptans*. The latter is currently the subject of a taxonomic and autecological investigation by Mrs E. L. Birse.

To the north of the loch is an extensive, though narrow, area of marsh with a typical complement of species such as *Filipendula ulmaria*, *Hippuris vulgaris*, *Triglochin palustris* and *Carex rostrata*. Part of this has been colonized by *Salix cinerea* ssp. *atrocinerea* and *S. viminalis*, with *S. caprea*, *S. purpurea* and *Alnus glutinosa* in small numbers (J. W. Kinnaird, personal communication).

The forward margin of the dunes is steep, but the presence of *Agropyron junceiforme* suggests that in some cases sand accumulates at the foot of the ridge. All stages of dune development and surface fixation are in evidence, including formation of a species-rich *Festuca rubra* turf with *Linum catharticum*, *Anthyllis vulneraria*, *Erodium cicutarium*, *Gentianella campestris* and *G. amarella* among others. Dune slacks are present, although not extensively developed, and to the north there is a low valley containing a rather sandy type of salt marsh including *Festuca rubra*, *Atriplex glabriuscula*, *Glaux maritima*, *Honkenya peploides* and *Plantago coronopus*.

Ornithology

The Loch of Strathbeg has been known as a famous site for birds for at least 150 years. In the first full account of its ornithology, published in 1854, Thomas Edward[5] lists most of the breeding species, and reports "that the common people who live thereabouts believe, and say it too, that all the birds of the world come there in the winter". In 1903 George Sim[6] reported that it is "the finest resort of wild fowl on the east coast of Scotland". In 1953 the Misses Baxter and Rintoul[7] recorded that it is "a wonderful sheet of water, large and shallow, holding a splendid variety of birds". Atkinson Willes describes why in his monograph[8] "many

Table 1 Averages and Maxima Recorded during Monthly Wildfowl Counts at the Loch of Strathbeg, 1954-1972

Number of counts		August	September	October	November	December	January	February	March	April	Total
1954–1963: Period	A:	1	7	8	6	4	4	5	5	1	41
1964–1972: Period	B:	—	8	9	9	8	9	6	5	—	54
Species											Maximum
Whooper Swan	A:	0	8	179	275	26	48	38	19	0	630
Cygnus cygnus	B:	—	X	328	166	82	75	106	86	—	822
Mute Swan	A:	224	220	184	139	141	62	113	58	22	269
Cygnus olor	B:	—	250	217	204	208	140	67	52	—	354
Greylag Goose	A:	0	2	201	345	311	434	191	120	9	1,166
Anser anser	B:	—	1	1,856	1,644	708	1,107	1,008	733	—	4,500
Pink-footed Goose	A:	0	5	712	411	51	76	194	418	1,050	2,000
Anser brachyrhynchus	B:	—	1	2,254	1,548	317	1,111	610	1,483	—	4,600
Mallard	A:	90+	507	1,198	2,047	2,634	3,715	1,990	771	386	8,000
Anas platyrhynchos	B:	—	360	822	1,713	2,276	2,135	1,337	406	—	6,515
Wigeon	A:	250	188	778	696	800	826	508	203	200	2,500
Anas penelope	B:	—	208	666	389	557	568	1,262	255	—	2,150
Pochard	A:	0	41	229	399	424	73	100	56	0	800
Aythya ferina	B:	—	39	973	1,073	361	424	416	156	—	2,764
Tufted Duck	A:	139	105	127	110	125	45	80	65	40	366
Aythya fuligula	B:	—	123	392	441	194	244	88	54	—	1,060
Goldeneye	A:	0	X	37	46	19	27	59	51	31	120
Bucephala clangula	B:	—	8	46	93	103	75	86	59	—	518

X, Recorded, average less than one.

factors combine to make this one of the greatest centres for wildfowl in Britain: first, the loch lies within a half mile of the sea in the easternmost corner of Scotland, and is thus most attractive to incoming migrants; second, it is large enough, with an area of 550 acres, to provide a secure roost, yet shallow enough to afford intensive feeding grounds; and last, the natural remoteness of the place is enhanced by careful keepering". Bourne[9] observed with radar that it was a focal point for bird movements in north-east Scotland, and he and Patterson[10] have described how Common Gulls *Larus canus* among other species follow the coast to the vicinity of Rattray Head before setting out over the sea when migrating from Britain to Scandinavia in spring. Elkins and Williams[11] have also reported the results of a long series of observations of seabird movements past Rattray Head lighthouse.

The wildfowl have now been counted once a month in the winter for 19 yr by two observers, the late Miss E. Garden and then Mr John Edelsten. The average number and maximum recorded for species where the total count has exceeded 500 are compared in Table 1. These counts are influenced by several variables, including the difficulty of counting the birds on such a large sheet of water, the tendency of geese to go inland to feed and ducks to retire to the sea when disturbed, and the fact that most of the birds are passing migrants or hard-weather visitors which only stay for a short time, all of which tend to result in underestimates of the number of birds visiting the loch. It will be seen, however, that except in the case of two surface-feeding duck which are present in greatest numbers in hard weather, of which there has been little in recent years, all species have tended to increase markedly during the period of observation in spite of a certain amount of controlled shooting. In general it now seems safe to say that at least 10,000 birds are normally present together during at least some stage of autumn passage every year, and many times this total, possibly as many as 100,000, may pass through, so that the loch

provides a vital staging post for migrants in an area where in fact there are few.

The vicinity of the loch is also one of the most important areas for breeding birds in north-east Scotland, where southern species such as in the past the Yellow Wagtail *Motacilla flava flavissima* have their northernmost breeding stations and overlap with those of northern species such as the Dunlin *Calidris alpina,* and there are at least eight, possibly ten, species of breeding duck. Mr N. Picozzi reports that during the recent five-year British Trust for Ornithology "ornithological atlas" survey ninety-two species likely to be breeding were recorded in this 10 km square, of which seventy-nine were proved to breed, compared with a maximum of eighty and sixty-seven and an average of sixty-five and fifty for the other fourteen squares in the north-east quarter of Aberdeenshire.

We thank the Wildfowl Trust, British Trust for Ornithology and Royal Society for the Protection of Birds for various ornithological data, and various members of the North-eastern Environmental Liaison Group, but especially Professor Kenneth Walton of the Geography Department, Aberdeen University, and J. A. Forster for information and comments on a draft of this note.

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Heavy Metals in British Waters

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Neither the number of areas contaminated with heavy metals nor the extent of the contamination seem to have changed much between 1960 and 1970.

THE programme of research and development on heavy metals in the marine environment, conducted by the Ministry of Agriculture, Fisheries and Food, has two chief objectives: first, the establishment and continued monitoring of concentrations in fish and shellfish of commercial importance in Britain to provide a basis for estimates of human intake of heavy metals[1,2] and, second, to provide data to assist an understanding of the behaviour of heavy metals when they are introduced into the marine environment—the factors determining their geographical distribution, or biological fate, including their effect, if any, on marine resources[3,4] and the kinetics of their metabolism in representative marine

organisms[5-7]. The first objective concerns short-term requirements for assessment and control of the present situation, whereas the second should provide a sound basis for a long-term policy of control, including the proper utilization of the capacity of the sea to accept such materials.

The result of a pilot survey of selected heavy metal concentrations in British coastal waters conducted during 1969 and 1970 was published last year[8]. This survey, and others conducted in 1971, was based on the sampling of both seawater and selected biological indicator materials (Fig. 1). The results of seawater sampling (Table 1) revealed that certain areas have elevated concentrations of some metals by comparison with the general levels prevailing in other areas. More detailed sampling using seaweed as an indicator confirmed that among these (Table 2) were the eastern Irish Sea (high values for Cu, Mn, Ni, Pb and Zn), the Severn Estuary (high values for Cd, Cu, Ni, Zn), the north-east coast round Seaham Harbour (Cd, Pb and Zn), and the Clyde in the vicinity of Hunterston (Cu, Mn and Ni). In these areas association with drainage from large industrial conurbations might well be invoked as a principal source of

Table 1 Concentrations (µg l.$^{-1}$) of Selected Heavy Metals in British Coastal Waters and the Adjacent North-east Atlantic (1970-71)

Element				British coastal waters			North-east Atlantic
		Area 1	Area 2	Area 3	Area 4	Area 5*	Area 4A
Zn	Geometric mean	2.0	3.0	4.2	2.0	3.3	3.0
	Range	1.2–3.8	0.8–9.0	2.3–7.5	1.3–3.4	0.8–8.8	1.4–7.0
	No. of observations	4	10	21	8	43	5
Fe	Geometric mean	0.3	0.09	0.18	—	0.06	—
	Range	0.06–1.3	0.03–0.6	0.06–1.9	—	0.06–1.5	—
	No. of observations	4	10	21	—	4	—
Mn	Geometric mean	0.32	0.53	1.95	0.18	1.5	0.06
	Range	0.10–0.49	0.15–2.6	0.22–14.6	0.02–0.49	0.24–15.9	0.03–0.09
	No. of observations	4	10	21	8	43	5
Cu	Geometric mean	0.46	0.59	0.66	0.34	0.82	0.26
	Range	0.23–1.29	0.18–3.75	0.28–0.98	0.19–0.62	0.24–1.9	0.05–0.80
	No. of observations	4	10	21	8	43	5
Ni	Geometric mean	0.38	0.38	0.71	0.53	0.84	0.43
	Range	0.22–0.95	0.22–0.55	0.32–22.9	0.36–0.79	0.16–5.4	0.29–0.66
	No of observations	4	10	21	8	43	5
Pb	Geometric mean	0.17	0.19	0.11	<0.05	0.21	—
	Range	<0.05–1.1	<0.05–1.2	<0.05–1.0	—	<0.05–0.8	—
	No. of observations	4	10	21	8	4	—
Cd	Geometric mean	0.06	0.11	0.04	<0.01	0.20	0.04
	Range	<0.01–0.38	<0.01–0.52	<0.01–0.62	<0.01–0.18	0.01–1.4	<0.01–0.41
	No. of observations	4	10	21	8	43	5

* J. W. Dutton, A. R. Folkard, P. G. W. Jones, and D. F. Jefferies, to be published.

the contamination. Some of these areas have also subsequently been reported by other authors to be areas of high ambient metal concentration[9,10]. Other relatively contaminated areas, not associated with such obvious pollution sources, were, however, found ; there are high levels of Zn in the western Irish Sea, and of Cd, Pb and Zn off the coast of North Wales. Here the chief contribution may be attributed to drainage from mineralized catchment areas.

Several other interesting findings were also made. First, and perhaps most significant, an analysis of seaweed samples collected a decade earlier, at the same positions as those used for seaweed sampling in the current survey, showed

Fig. 1 Principal seawater sampling areas in British coastal waters. ■, Sampling points for *Fucus* spp.

overall no significant differences in concentration with the exception of cadmium (Table 3). This suggests that the metal pollution situation as a whole has changed little, if at all, in location or magnitude during that period : indeed, the concentrations of cadmium may on average have fallen. Second, the current survey showed an attenuation of concentration offshore, the high concentrations being virtually a thin skin round the margins of the sea areas examined. The concentrations in open seawater, even of areas such as the Irish Sea and the North Sea, are not, except in isolated instances, significantly different from those in the open Atlantic Ocean adjacent to the British Isles (Table 1). Third, in the Irish Sea, where distributions with respect to depth were examined, no significant difference in metal concentration in filtered seawater samples was found between surface, midwater and bottom, indicating thorough mixing in this shallow sea area.

The later and more detailed examination of the situation in the North Sea carried out during 1971, including both

Table 2 Derived Concentrations (µg l.$^{-1}$) of Selected Metals in Shoreline Seawater of "Hot Spot" Areas, Based on Seaweed Sampling, Compared with North-east Atlantic Seawater (1970)

Location	Cd	Cu	Mn	Ni	Pb	Zn
Eastern Irish Sea	0.6	3.6	4.4	3.0	2.3	26.6
Severn Estuary	7.7	4.6	2.1	6.4	1.5	22.2
Tyne-Tees (Seaham Harbour)	0.8	3.3	2.5	2.7	2.2	11.7
Clyde (Hunterston)	0.6	2.8	8.2	3.0	1.8	6.2
Atlantic (cf. Table 1)	0.04	0.26	0.06	0.43	0.02*	3.0

* Open ocean concentration[11]—value from IDDE Baseline Conference.

seawater and seaweed sampling, confirmed the interpretations of the previous survey, namely that in general elevated concentrations are restricted to the margins and to confined localities largely associated with industrial development. It also showed that the North Sea coastal water was on average about as contaminated as the east Irish Sea, the area previously revealed as having the highest average concentrations of most of the metals examined. Elements of this

North Sea programme are being conducted as part of an international study of pollution in the North Sea under the auspices of the International Council for the Exploration of the Sea. The study, which is being jointly carried out by

Table 3 Comparison of Heavy Metal Concentrations in *Fucus* Seaweed from Britain (1961 and 1970)

Element	Geometric mean quotient	t	P
Cd	0.68	3.32	>0.01
Cu	0.90	1.34	<0.2
Fe	1.03	0.27	<0.7
Mn	0.86	1.68	<0.1
Ni	0.94	0.70	<0.4
Pb	0.82	1.28	<0.2
Zn	0.90	0.94	<0.3

Significance testing of the logarithm of the quotient metal concentration (1970)/metal concentration (1961).

member states whose coastlines abut the North Sea, was undertaken at the initiative of the Ministry of Agriculture, Fisheries and Food following a request from the United Nations Food and Agriculture Organization Technical Conference on Marine Pollution. Apart from the work already described, this study also includes an examination of heavy metal concentrations in representative commercial fish species and a compilation of sources and magnitudes of inputs. Other aspects are concerned with pesticides and halogenated hydrocarbons.

The data from British coastal waters and the results of the monitoring of commercial fish species have also been contributed to the Environmental Quality Programme of the United States International Decade of Ocean Exploration (IDOE). This programme, which is supported by the National Science Foundation, is part of the overall United

Table 4 Mean Concentrations ($\mu g\ g^{-1}$ Wet Weight) of Metals in the Muscle of Fish Landed in England and Wales from Selected Sea Areas

Origin	Cd	Cu	Hg	Pb	Zn
English and Welsh coasts (less than 25 miles from the coast)	0.11	0.95	0.29	0.66	5.52
Irish Sea (more than 25 miles from the coast)	0.07	0.80	0.21	0.50	5.70
North Sea (more than 25 miles from the coast)	0.12	<0.50	0.10	<0.50	4.83
Distant water (Iceland, Barents Sea, Norway Coast)	<0.05	1.80	0.06	<0.50	6.10

States contribution to the Intergovernmental Oceanographic Commission's long-term and expanded programme of oceanic exploration and research (LEPOR), aspects of which are concerned primarily with marine pollution, which was recognized, when formulating the programme, as an important area requiring further research.

The IDOE environmental quality programme has so far been largely concerned with establishing pollutant baselines for the Pacific, Gulf and Atlantic coasts of the United States. The British data on metals were contributed to provide a complementary picture for part of the eastern seaboard of the Atlantic. The general conclusions from both sets of

data[11] are very similar, namely, elevated concentrations are largely restricted to estuaries and the narrow coastal margin, and are associated with drainage from industrial areas or the dumping of sewage sludge and industrial wastes. It has been recommended that the United States programme should place continuing emphasis on research in coastal waters and estuaries by virtue of their elevated metal concentrations and the importance of the fishery resources involved.

In summary, the results of seawater sampling on a pilot scale around the British Isles show that contamination is restricted to a few areas, chiefly, but not exclusively, linked to industrial development, and that even in these areas contamination does not spread very far offshore. Neither the number of contaminated areas nor the magnitude of the contamination seems to have changed much between 1960 and 1970. Furthermore, the monitoring of commercial fish species[12] shows that, except in the case of sedentary shellfish, variations in inshore seawater metal concentrations are not reflected to any great extent in the edible portions of these species (Table 4). Fish are mobile, and the timescale of their metal turnover smooths out temporal and spatial variations in seawater concentrations. Of course concentrations in inshore fish are sometimes higher than those in offshore fish, especially in the case of Cd, Hg and Pb. This strongly indicates that metal pollution problems are essentially national or regional problems, with the possible exception of the lead problem as atmospheric transportation is an important contributory factor. Their control and monitoring can thus best be met by national or perhaps regional action. The deep-sea dumping of waste is a minor contribution to metal pollution and, moreover, is likely to be brought under international control very soon[13-15].

In the future, attention will continue to be directed towards the monitoring of pollutant concentrations and inputs, in order to provide a basis for regulating discharges to a level commensurate with acceptable concentrations in those biological materials judged to be critical in the context of public health or resource damage. There is also an outstanding need for better data about acceptable standards for human and resource exposure, and in particular better methods for assessing the significance of metal concentrations for marine organisms at concentrations appropriate to the environmental situation, that is long-term exposure to low concentrations, need to be developed.

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Descent of Lithosphere beneath New Hebrides, Tonga-Fiji and New Zealand: Evidence for Detached Slabs

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Study of seismic wave propagation in the mantle beneath the New Hebrides island arc shows that the remarkable gap in seismic activity between deep and intermediate depth earthquakes at the northern part of the arc corresponds to a gap in the lithospheric slab descending beneath the arc: the deep earthquakes mark a detached piece of lithosphere. Although observations for New Zealand deep earthquakes are ambiguous, other evidence suggests the detachment of lithosphere beneath New Zealand.

ONE of the outstanding features of the distribution of earthquakes in the upper mantle is the existence of gaps in seismic activity between depths of about 300 and 550 km. These gaps are prominent beneath South America, New Zealand, and the New Hebrides island arc. They are of great interest because of the implication that portions of lithosphere can break off from the descending plate and exist as isolated slabs within the mantle.

Here we present evidence from study of seismic wave attenuation for the detachment of lithospheric slabs in the upper mantle beneath the New Hebrides arc. Detachment is also indicated by travel time data and reconstructions of the past movements of plates in the region. We concentrate on the study of seismic attenuation because the effects are large and easy to observe and interpret[1-3].

Isacks and Molnar[4] suggest that the gaps in seismic activity as a function of depth can be explained by two models. In the first the stress inside a continuous slab varies from down-dip extension at intermediate depths to down-dip compression at greater depths, and thus is near zero between these depths. In the second a piece of descending lithosphere breaks off, sinks into the upper mantle and leaves a gap between the piece and the plate to which it was attached. The character of seismic waves, especially shear waves, produced by deep earthquakes and recorded at stations along island arcs where large gaps in seismic activity exist provides evidence for determining which of these models is correct. Observation of attenuated, low frequency waves for the appropriate paths indicates a gap

in the descending lithosphere. But if high frequency shear waves are observed, then the interpretation is ambiguous. The observations can be explained either by propagation along a continuous high Q lithospheric slab or by propagation through the upper portion of a discontinuous slab that provides a low attenuation path through the asthenosphere. The second explanation implies that for 1-3 Hz shear waves attenuation is small below depths of about 300 km.

The New Hebrides island arc provides a unique opportunity to study the nature of the gap in seismic activity in the upper mantle. Seismograph stations are well distributed along the arc. The gap is well established between depths of about 300 and 600 km. The structure of the intermediate and deep seismic zones with the very steeply dipping intermediate zone and the approximately horizontal deep zone certainly suggests that the two zones may not be connected. Enough deep earthquakes have occurred since the stations were installed to provide a large sample of paths. Forty deep earthquakes in the 10 year period 1961-1970 were recorded at Noumea (NOU) and Port Vila (PVC) stations (Fig. 1). Lonorore (LNR) was established in 1968. NOU, PVC and LNR employ 1 Hz underdamped seismometers and 2 Hz overdamped galvanometers. The instruments have a relatively flat response for seismic wave frequencies between 0.5 Hz and 10 Hz and thus record very clearly the large variations of shear wave fre-
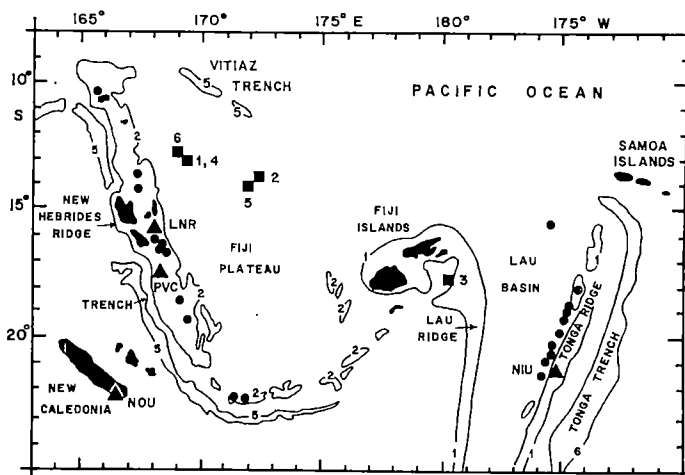
Fig. 1 Map showing the Tonga–Fiji–New Hebrides region of the southwest Pacific. ●, Historically active volcanoes; ▲, seismic stations; ■, locations of deep earthquakes used in Figs. 2 and 3. Water depths are in km.

quencies. Detailed description of the New Hebrides–New Caledonia seismic network is given by Dubois[5].

The inclined seismic zones of South America also have remarkable gaps in seismic activity between about 350 and 550 km. A detailed study of the records produced by almost all the South American deep earthquakes that occurred during the past 10 yr at stations along the western coast of South America is currently under way, and will be reported in a separate study.

Lithospheric Gap in New Hebrides Arc

Fig. 1 shows the location of the stations in New Caledonia and New Hebrides used in this study. We have examined all the records produced at these stations by the New Hebrides deep earthquakes. The most striking observation is that predominantly low frequency (about 0.5 Hz) S waves are recorded at PVC and LNR from the deep earthquakes north of 15° S.

Fig. 2 shows a cross-section through the New Hebrides arc that intersects NOU, LNR and passes close to PVC. New Hebrides deep earthquakes located at the western part of the deep zone (very close to the downward projection of the intermediate depth zone) produce attenuated, low frequency S waves at PVC. The ray paths pass just beneath the dipping seismic zone. Frequencies greater than 1 Hz are absent and the amplitude of the S phase is generally less than that of P phase. As Oliver and Isacks[1] and Barazangi and Isacks[3] show, this can be explained by a transmission through an attenuating low Q zone. In contrast, S waves recorded at NIU station on the Tonga island arc from Tongan deep earthquakes have predominant frequencies of 3–4 Hz and the amplitudes of S are generally larger than those of P.

Deep earthquakes also produce low frequency shear waves at LNR, a station close to the active volcanic line of the New Hebrides arc. This is in marked contrast to the observation of high frequency S waves from Tonga deep earthquakes at stations along the active volcanic line of the Tonga arc[6].

We interpret the observation of low frequency S waves at PVC and LNR to be mainly the result of attenuation along the path. The effect of the source can be excluded since New Hebrides deep earthquakes produce seismograms at Fiji stations that are similar to those produced by the Tonga deep earthquakes (the New Hebrides and Tonga deep earthquakes are approximately equidistant from the Fiji stations). The effect of the station can be excluded since intermediate earthquakes located along the New Hebrides arc produce, without exception, high frequency (about 3–4 Hz) S waves at PVC and LNR. This is so even where the path lengths are comparable or greater than those from the deep earthquakes. Further, the Tonga deep earthquakes produce seismograms at PVC and LNR that are strikingly similar to those produced at the Fiji stations. Thus, attenuation along the path is the main cause for the observed low frequency S waves at PVC and LNR.

The attenuation is chiefly below 300 km, judging by the abundant observations of high frequency shear waves from intermediate depth earthquakes to PVC and other New Hebrides stations. All observations taken together are best explained by the absence of lithospheric slab material between depths of about 300 and 600 km; the deep earthquakes of New Hebrides therefore represent a detached slab in the upper mantle. To our knowledge, this is the first direct evidence that the attenuating, asthenospheric layer is deeper than about 300 km in the upper mantle.

New Hebrides deep earthquakes always produce low frequency S waves at NOU (Fig. 2). This is most probably due to attenuation in the upper mantle (the asthenospheric layer), because the ray paths to NOU completely miss the dipping New Hebrides seismic zone.

New Hebrides deep earthquakes located at the eastern part of the deep zone produce attenuated, low frequency S waves at PVC and LNR. The ray paths, calculated for a laterally

homogeneous mantle with a Jeffreys–Bullen (J–B) velocity structure, pass just above the inclined seismic zone (Fig. 3). S phases which similarly appear to pass above the Tonga inclined zone, however, have large amplitudes and high frequencies (we note that the time scale of NIU record is about twice that of PVC, as shown in Fig. 3). Even though the J–B ray path seems to miss the Tonga seismic zone, the high frequency S waves probably travel through the descending slab. Barazangi, Isacks and Oliver[7] describe other evidence that the slab descending beneath Tonga acts as a wave guide for high frequency shear waves and is therefore continuous. Thus by comparison the absence of these high frequency shear waves for the easternmost New Hebrides deep earthquakes can be taken as evidence for the detachment of lithosphere beneath the New Hebrides.
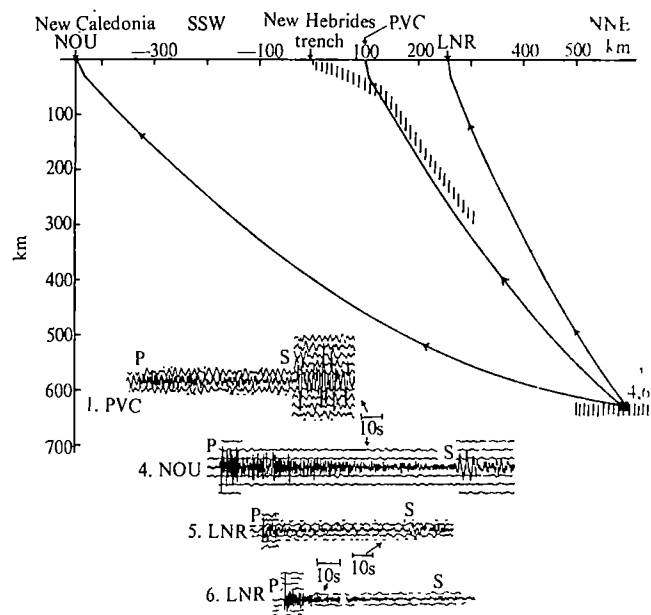
Fig. 2 Cross-section of the New Hebrides arc showing J–B ray paths to NOU, PVC and LNR stations and the corresponding records [E–W component at PVC, N–S component at NOU, and Z component at LNR] and the locations of seismic activity (vertical lines). Only low frequency S waves are recorded at the stations.

We will present a detailed study of the travel times of P waves of the New Hebrides deep earthquakes later. The travel time residuals of P waves of the New Hebrides deep earthquakes at PVC and LNR stations along the arc are close to normal (about 1 to 2 s earlier). This is in contrast to P residuals of about 4 to 5 s earlier from the Tongan deep earthquakes recorded at stations along the Tonga arc[8]. Thus the travel time data support those obtained from seismic wave attenuation and indicate that the deep earthquakes at the northeast of the arc represent a detached lithospheric slab.

During the past seven years three deep earthquakes occurred south of 15° S, south of the horizontal oblong-shaped zone, and are located along a line parallel to the southern part of the New Hebrides arc (Fig. 5). Records produced by these earthquakes at NOU in New Caledonia and at stations located in the northern part of the New Hebrides arc (to the north of about 16° S latitude, LNR and LUG) show attenuated, low frequency S waves. But records produced at PVC from the most recent event located at about 18° S and 173° E show large amplitude, high frequency S waves. This is the only one of the three shocks recorded at PVC with good quality records. This observation is quite clear, however, and may imply the continuity of the descending slab in the southern part of the New Hebrides arc. More data are required before a meaningful interpretation can be made for the southern deep earthquakes zone.
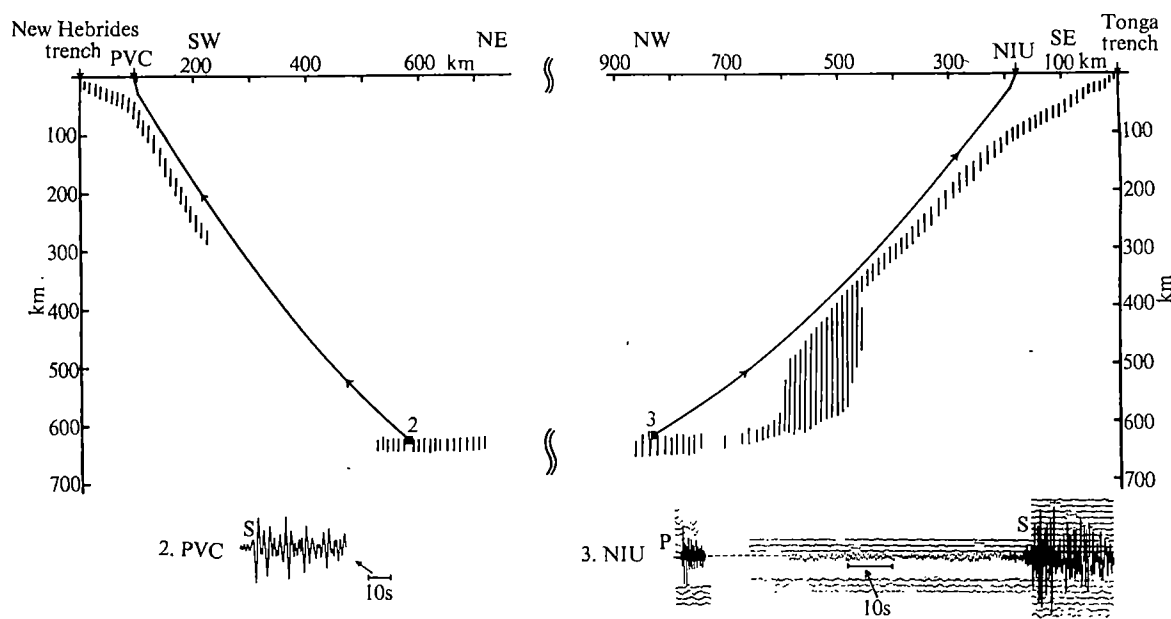
Fig. 3 Two cross-sections of Tonga and New Hebrides arcs showing ray paths to NIU and PVC stations and the corresponding records [E–W component at PVC, and Z component of P, and N–S component of S at NIU] and the locations of seismic activity in the upper mantle (vertical lines). Note the great difference in the signature of S waves at NIU and PVC in spite of the similarity in ray paths (time scale of NIU record is about twice that of PVC).

Detached Piece of Lithosphere beneath New Zealand?

In New Zealand earthquakes reach a depth of about 300 km in the North Island and about 200 km in the northernmost part of the South Island. In addition three earthquakes occurred at depths of about 600 km in 1953 and 1960 beneath the North Island[9]. Fig. 4 shows a cross-section of the New Zealand arc and examples of seismograms from the local New Zealand network. Deep earthquakes produce high frequency S waves at Wellington (WEL). Two quite different explanations can be made for this. One is that the slab beneath New Zealand is continuous and reaches depths of at least 600 km, and thereby provides a path for high frequency S waves. The second is that although the slab may have a gap beneath about 300 km, the portion above 300 km is sufficient to provide a "window" through the zone of high attenuation. This second explanation implies that the principal zone of attenuation is located above 300 km, and thus implies a significant difference between the New Zealand and New Hebrides regions with respect to attenuation below 300 km.

The second alternative, that a detached lithosphere is present beneath the North Island of New Zealand, is supported by the variation of down-dip length of the inclined seismic zone as a function of latitude along the New Zealand–Kermadec–Tonga plate boundary. If New Zealand deep earthquakes are excluded, the down-dip length increases regularly northward as predicted by locations of the pole of relative motion between the Australian and Pacific plates[10,11]. The New Zealand deep shocks are thus distinctly anomalous in this respect and seem to mark a detached piece of plate.

New Zealand deep earthquakes produce low frequency, attenuated S waves at Tarata (TNZ) and Onerahi (ONE) which are located to the west of the line of active volcanoes in the North Island. Mooney[12] mapped a zone of anomalously high attenuation in the uppermost mantle also located west of the active volcanoes. Thus, the low frequency S waves at TNZ and ONE are probably the result of attenuation in the uppermost mantle to the west of the dipping seismic zone.

An interesting observation is that New Zealand deep shocks produce high frequency S waves at stations in the South Island. Fig. 4 shows an example recorded at Gebbies Pass (GPZ), a station located along the aseismic[13] east coast of

the South Island. This observation suggests that beneath at least the northern part of the South Island no major zone of attenuation is present. The lithosphere marked by intermediate depth earthquakes beneath the North Island may thus extend beneath part of the South Island.

Deep Earthquakes beneath Fiji

An unusual feature of the earthquake distribution in the Tonga–Fiji region is the occurrence of deep earthquakes west
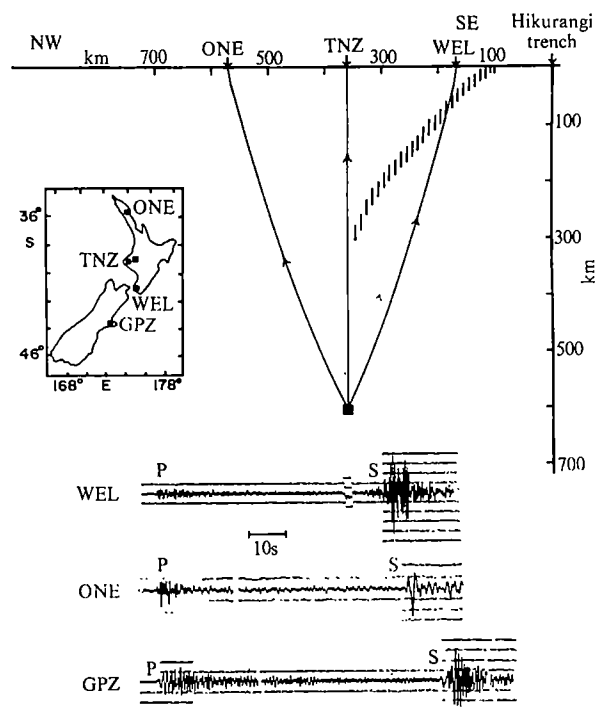
Fig. 4 Cross-section of the New Zealand arc showing ray paths to WEL, TNZ and ONE stations, horizontal records to WEL, ONE and GPZ stations, and the dipping seismic zone beneath the North Island (vertical lines). Insert map shows the locations of stations (●) and the location of the deep earthquakes of New Zealand (■).
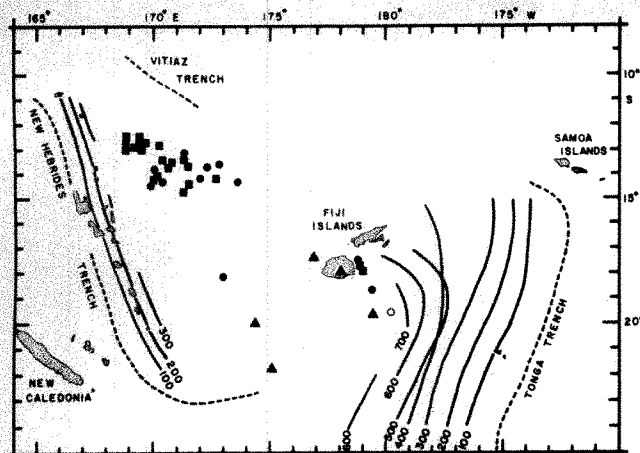
Fig. 5 Map showing contours of earthquake depths for Tonga and New Hebrides arcs, the deep seismic zone of New Hebrides, and well located deep earthquakes beneath the Fiji islands and the Fiji plateau. ▲, Events with depth range between 525 and 575 km; ●, events with 576 to 625 km depth; ■, events with 626 to 675 km depth. The open circle represents an event with a depth of 470 km.

of the inclined seismic zone of the Tonga arc (Fig. 5). In the past 10 yr about 8 well located deep earthquakes occurred beneath the Fiji Islands. It is not clear whether these earthquakes represent a continuation of the descending Tonga slab, a slab(s) detached from the present descending slab, or a slab detached during an earlier episode of underthrusting. Evidence obtained from focal mechanisms by Isacks et al.[14] suggests that these earthquakes represent a contorted continuation of the northern edge of the descending Tonga slab. In any case these earthquakes and the New Hebrides deep earthquakes show a considerable horizontal extent away from the corresponding descending slabs. This suggests that the earthquakes mark lithospheric slabs that are unable to penetrate the 600–700 km discontinuity of the upper mantle, and hence the

discontinuity may represent the lower limit of the asthenosphere. These slabs may pile up above the discontinuity until their assimilation in the mesospheric lower mantle.

Overall Model

The New Hebrides and New Zealand deep earthquakes mark detached pieces of lithosphere in the upper mantle; considerable seismic wave attenuation probably exists below about 300 km of depth in the upper mantle beneath the northern part of the New Hebrides arc, which implies that the asthenosphere may extend deeper than 300 km in the mantle in this region; the spatial distribution of deep earthquakes between the New Hebrides and Tonga arcs suggests that slabs of lithosphere are unable to descend beneath about 700 km in the mantle.

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Effect of Magnesium on Horizontal Cell Activity in the Skate Retina

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Magnesium, like light, hyperpolarizes retinal horizontal cells. In the dark, horizontal cells seem to be depolarized by neurotransmitter released continuously from photoreceptors.

THERE is both anatomical and physiological evidence to suggest that synaptic transmission between vertebrate photoreceptors

and second-order retinal neurones (horizontal and bipolar cells) is chemically mediated. The aggregation of vesicles in the receptor terminals[1], the separation between junctional membranes[2,3], and the latency differences between pre- and postsynaptic responses[4] are consistent with this view. Although identification of the neurotransmitter has yet to be made, studies on the properties of horizontal cells have led to the interesting suggestion that the photoreceptor releases a depolarizing transmitter in the dark and that light decreases the flow of this substance[5-8]. For example, horizontal cells exhibit low resting potentials (25–40 mV)[9,10], and most of

these cells only hyperpolarize in response to light[9]. Furthermore, an increase of input resistance of the horizontal cell often accompanies light stimulation[11], and transretinal currents that depolarize the receptor terminals induce a depolarizing response in the horizontal cells[5-8]. Recent studies on vertebrate photoreceptors have also provided results compatible with this notion. In darkness there is a steady inward sodium flux across the plasma membrane of the rod outer segment; light decreases the sodium conductance of the outer segment, thereby hyperpolarizing the receptor[8,11,12]. Thus, the receptors are partially depolarized in the dark, a finding consistent with the suggestion of neurotransmitter release in darkness.

We have tested this hypothesis by determining the influence of magnesium on the electrical properties of skate horizontal cells (either *Raja erinacea* or *R. oscellata*). We assumed that, as at other chemically-mediated synapses, high levels of extracellular magnesium block neurotransmitter release from the presynaptic (that is receptor) terminal[13-15]. Intracellular recordings from horizontal cells were obtained from the eyecup preparation with glass micropipettes filled with 2 M KCl and having resistances of 35–55 Mohm when measured extracellularly in the tissue[10]. Signals were led from the micropipettes to a Bak ELSA-4 negative-capacitance amplifier via Ag-AgCl electrodes, observed on an oscilloscope, and recorded on a Brush (model 280) penwriter. In addition, recordings of the electroretinogram (ERG) were obtained with a partially insulated Ag-AgCl wire placed in the vitreous humour. ERG responses were amplified, displayed and recorded conventionally[16,17]. After impaling a horizontal cell, a drop of elasmobranch Ringer[18], in which 100 mM MgCl was substituted for 100 mM of NaCl, was gently pressure-ejected onto the surface of the retina. Recordings were obtained before, during, and after exposure to the high magnesium Ringer.
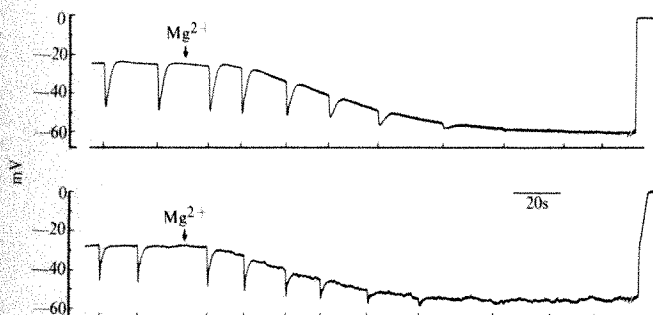
Fig. 1 Two experiments showing the effects of magnesium on skate horizontal cells. A drop of Mg-Ringer was applied to the eyecup (arrows), and within 15–25 s the cells began to hyperpolarize. Over the next 3 min, the cells hyperpolarized to a level of about −60 mV and light evoked activity was lost. A break in the trace indicates the time at which the pipettes were withdrawn from the cells. The rapid, positive shifts of potential of 55 to 60 mV confirmed the increase in membrane potential of the horizontal cells in the presence of high levels of magnesium. Flash intensity (filter density of 5.5) and duration (0.2 s) were kept constant throughout both experiments. The markers along the lower trace of each record indicate flash preparations.

Fig. 1 shows the effects of the test solution (Mg-Ringer) on two horizontal cells. Resting potentials of 25 and 30 mV were recorded initially in the two cells and light flashes of constant duration and intensity gave hyperpolarizing responses of 15–20 mV. The test stimuli were about 1.5 log units above threshold; flashes of saturating intensity evoked responses of 25–30 mV in these cells.

About 15–25 s after a drop of Mg-Ringer was applied to the eyecup (arrows, Fig. 1), the membrane potentials of the horizontal cells began to hyperpolarize and there was a corresponding decrease in the amplitudes of the light-evoked responses. Within 3 min, the membrane potentials had fallen to about −60 mV and the response to light was abolished. In these two experiments, the micropipettes were withdrawn from the cells after the resting potentials had stabilized. Positive shifts of potential of 55–60 mV signalled the exit of the pipettes from the cells and confirmed the intracellular measurements of large membrane potentials in the presence of high magnesium.
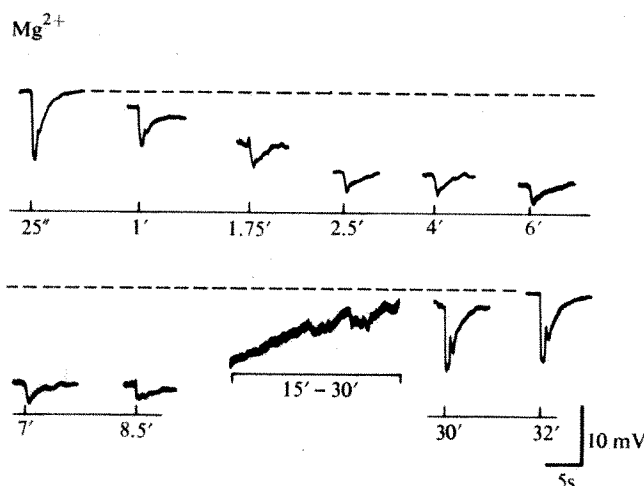
Fig. 2 Long-term recordings illustrating the transient nature of the effects of magnesium on skate horizontal cells. The times after the application of the test solution at which light stimuli were presented are indicated along the lower trace. The level of each trace relative to the dashed line shows the extent to which the cell was hyperpolarized. The cell was not completely hyperpolarized by the drop of test solution, so a small response could be elicited even after 8.5 min. Between 15 and 30 min (shown on the contracted time base) the membrane potential of the cell depolarized, and the responses at the end of this time had returned to normal amplitudes.

These results strongly support the notion that skate horizontal cells are maintained in a partially depolarized state in the dark, because of continual release of a depolarizing neurotransmitter from the photoreceptors. On this view, high magnesium, like light, decreases the release of neurotransmitter and the horizontal cell hyperpolarizes. As the horizontal cells hyperpolarize in response to a high magnesium environment, there is a distinct increase in baseline fluctuations. This is particularly evident in the lower record of Fig. 1. It is possible that these fluctuations indicate the presence of spontaneous miniature postsynaptic potentials in the horizontal cells, which are uncovered in conditions of high extracellular magnesium. In muscle it has been shown that miniature endplate potentials persist in the presence of high magnesium[19,20].

The effects of a drop of Mg-Ringer on the eyecup preparation are transient. Fig. 2 illustrates an experiment in which a horizontal cell was monitored for more than 30 min after the test solution was added to the eyecup. In this experiment the horizontal cell did not fully hyperpolarize and light-evoked responses were not entirely abolished. After application of the Mg-Ringer for 30 s, the membrane potential of the cell became more negative and responses to light decreased in amplitude.

After 3–5 min the resting potential stabilized, and only small light-evoked potentials could be recorded. For the next 5–10 min, no significant changes were noted. Between 15 and 30 min, however, the horizontal cell membrane depolarized to its former level (~ -30 mV) and light-evoked activity regained its original amplitude.

Earlier experiments by Svaetichin and his colleagues[21,22] showed that anoxia and a variety of metabolic poisons produce effects on horizontal cells similar to those reported here. Some of these agents may exert their effects by disrupting synaptic transmission, but others may inactivate the receptors as well. The ERG was not monitored in those experiments; no information on receptor activity in the presence of the agents was provided.

I_T

Mg^{2+}

$100 \mu V$

$5s$
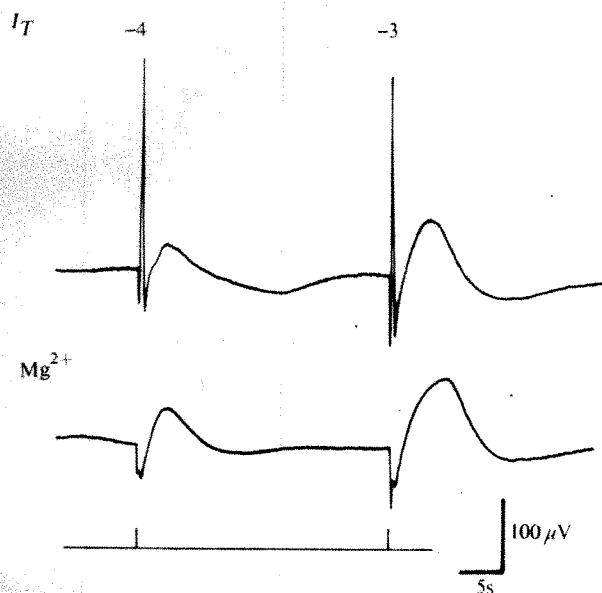
Fig. 3 The effects of Mg-Ringer on the skate electroretinogram (ERG). The upper traces show the principal components of the response at two flash intensities (filter densities of 3 and 4) in the normal ERG. The initial negative deflexion (a-wave) is followed by the large positive b-wave and a slow c-wave of lower amplitude. Magnesium almost entirely abolished the b-wave, but a- and c-waves are virtually unaltered.

Fig. 3 shows ERG recordings at two intensities ($I_t = -3$ and -4) before and 15–20 min after the Mg-Ringer was applied to the eyecup. The a- and c-waves show little alteration in the presence of high magnesium, but the b-wave is almost entirely abolished[23]. The leading edge of the a-wave of the ERG is derived from photoreceptors[24], whereas the c-wave originates in the pigment epithelium[25] but depends on receptor activity for its generation[26]. The b-wave, on the other hand, arises proximally to the receptors[24,27]; its selective loss in the presence of high magnesium is to be expected if transmission between photoreceptors and second-order neurones is blocked. In some experiments, a small loss in amplitude of a- and c-waves was noted; this was probably due to the one-third reduction in Na^+ concentration in the Mg-Ringer[28]. As we have said, the effects of a drop of Mg-Ringer on the eyecup preparation are transient; the tiny b-waves seen in the responses obtained 15–20 min after the test Ringer was applied to the preparation represent the initial stages of b-wave recovery.

The likelihood that vertebrate photoreceptors secrete a depolarizing transmitter in darkness raises two questions. The first concerns the mechanisms by which bipolar cell responses of opposite polarity are produced by the action of a depolarizing transmitter. The hyperpolarizing bipolar cells exhibit an increase in membrane resistance during light stimulation[8,29], and thus generation of these responses may be similar to that of horizontal cell potentials. The depolarizing bipolar cells pose a more difficult problem. Nelson has recently found that the photic responses of these cells in the mudpuppy (*Necturus*) are accompanied by a decrease in membrane resistance[29]. If these bipolar cells also receive their input directly from receptors, this finding implies that the effect of the neurotransmitter is to decrease conductance of the cell. Although unconventional action for a neurotransmitter, recent experiments suggest that this does occur in cells of the frog sympathetic ganglion[30]. Alternatively it is possible that depolarizing bipolar cells do not receive direct synaptic input from receptors, a suggestion that has already been made by Tomita[8].

The second question concerns the identification of the photoreceptor neurotransmitter. It has been shown that certain amino-acids rapidly depolarize skate horizontal cells[17,31,32]. L-Na aspartate is especially potent in this respect (see Fig. 2 in Dowling and Ripps[17]), and might be considered as a possible candidate for the photoreceptor transmitter. It is noteworthy that recent work indicates that L-glutamate is the probable neurotransmitter at electroreceptor synapses in the skate[33].

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LETTERS TO NATURE

PHYSICAL SCIENCES

Tracks from Extinct Radioactivity, Ancient Cosmic Rays, and Calibration Ions

WE present here an alternative explanation of the fossil tracks in lunar minerals that have been attributed[1,2] to extinct radioactivity of superheavy elements.

Particle track etching of crystals from extraterrestrial materials has yielded a wealth of information about cosmic rays and spontaneously fissioning nuclides, and consequently about nuclear synthesis, early Solar System history, and the origin and history of cosmic rays. The lengths of tracks from cosmic ray nuclei that penetrate meteorites can be used to measure the abundances of heavy cosmic rays[3,4] and these tracks can be distinguished by various features from tracks caused by fission[3,5,6]. Simple means of measuring the full track lengths have been developed by Lal et al.[7] and used to infer detailed cosmic ray abundances.

In applying this technique to lunar and meteoritic samples Bhandari et al.[1,2] assumed (reasonably) that the most abundant tracks (those of length 11 to 12 μm) were from Fe nuclei. Uranium-235 fission tracks were shown to have lengths ~14 to 15 μm and the observed excess of natural tracks of that length over what could be expected from the uranium concentration present was attributed[1,2] to the past decay of now extinct [244]Pu, a nuclide which existed early in the history of the Solar System[5,6,8]. Tracks of ~25 μm length then became an anomaly, which Bhandari et al.[1,2] attributed to the fission of now extinct superheavy nuclei (nuclear charge ~100-114, atomic mass ~300). Such nuclei would be expected to produce unusually long tracks[9].

The positive identification of superheavy elements, if confirmed, would be a remarkable culmination of a sequence of searches by many workers, using a variety of techniques that have yielded no positive results which have survived careful examination. But it is a far from trivial task to identify in this manner a minority segment of the fission, which is itself a small component within a large cosmic ray background. In particular the first attempts to infer the length of fresh tracks of Fe nuclei using accelerator ions indicated a probable length[10] that was greater than that observed for the most abundant natural tracks in extraterrestrial crystals.

More direct, recent results[11,11a] have shown a clear discrepancy to exist. In the first of these works a beam of Fe ions of 10 MeV/nucleon allowed the full, etchable track lengths to be measured: the distribution is peaked at 19 to 21 μm cm with a bell shaped distribution in lengths ranging from 12 to 24 μm cm in lunar pyroxene and meteoritic enstatite. In the second of these works fresh, natural iron-group tracks in a feldspar crystal that had been exposed to solar cosmic rays on the Apollo 16 mission were found to extend up to 30 μm in length. In contrast the lunar tracks were most abundant at significantly shorter lengths (13 or 15 μm) and were even less sharply peaked than was the distribution of calibration tracks.

Either the natural tracks that were previously inferred to be Fe are in fact lighter nuclei, or some mechanism has shortened the Fe tracks. In principle the more abundant tracks could be the lighter, spallation products of iron produced by nuclear interactions within the meteorite or lunar sample. Because the interaction mean free path for iron is ~6 cm of rock[3], this alternative would require that the 11 to 12 μm peaks would always have been seen in samples from depths appreciably greater than that; that is not the case. In addition, direct experiments[12] as a function of depth at lesser depths show the 11 to 12 μm peak.

We turn therefore to the alternative that the most abundant tracks are Fe, but that they have been altered over time. Two mechanisms are known for track alteration: heating[13] and deformation[14]. The first is far more extensively documented. Based on the extrapolations of laboratory annealing experiments, tracks in most meteoritic and lunar crystals exposed to the expected temperatures should be stable and unaltered[3,11,13,15] throughout their cosmic ray exposure times. If the usual exponential form of annealing kinetics were to break down by the intervention of a second mechanism with a lower activation energy, it would be possible for annealing to occur. Such a behaviour has, for example, been observed on one occasion for argon diffusion in mica[16]. But such a result has never been obtained for track annealing in the many cases where the kinetics have been measured[17]; in short there is no evidence for such an effect.

In contrast there is evidence for mechanical effects. Most samples from the lunar surface have been exposed to shock— the agency that broke them up from larger rocks. Similarly meteorites have been bombarded in space and end their cosmic ray exposure by experiencing high pressures as they encounter the Earth's atmosphere; finally, the larger surviving fragments are shocked by impact with the ground. We have observed track shortening for cosmic ray tracks in deformed lunar pyroxenes[14] and track fading and erasure for uranium fission fragment tracks both in individual minerals shocked in the laboratory[18] and in natural rocks that were exposed to shock conditions (unpublished). We have now measured fission fragment track lengths as a function of shock pressure for apatite taken from granodiorite shocked to pressures of 11, 13, 20 and 30 kbar (unpublished). We find that the median track lengths on a polished section are 5.5, 5.4, 2.7 and 1.5 μm at the four pressures. The corresponding maximum track lengths on a polished section are 9.5, 12.0, 8.8 and 6.5 μm. (In contrast biotite shocked normal to the layer planes shows less than a 10% shortening up to 92 kbar.) Of these two results the minerals from shocked rock are the more directly pertinent, since they more closely simulate the shock conditions to be expected in lunar and meteoritic samples.

To summarize, track lengths are decreased in a manner consistent with the shift of most observed natural cosmic ray tracks in crystals[1,2,11,12] relative to the calibration Fe tracks[11,11a]. If this explanation is tentatively accepted, then the longer tracks observed by Bhandari et al.[1,2] and attributed to fission of [244]Pu and superheavy nuclei would be explained most directly as normal, unaltered cosmic ray Fe or Ni tracks that have been formed since the last shock event that produced shortening of tracks. Further and more direct evidence of shock of the particular pyroxenes used by Bhandari et al.[1,2] might be obtainable by examination, using transmission elec-

tron microscope replicas, of their samples etched with the acid etch that has been shown to reveal deformation markings[19].

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Radio Pulses from the Direction of the Galactic Centre

WEBER[1-3] has reported detecting pulses of gravitational radiation. The flux density per event is about 3×10^5 erg cm^{-2} s^{-1} Hz^{-1} at 1,660 Hz, implying a possible release of 10^{54} erg, equivalent to about 1 $M_\odot$, if the radiation originates in the region of the Galactic centre. It has been suggested that if only 1 part in 10^{25} of the energy were radiated in the electromagnetic spectrum, this could be detected. Some attempts have been made at radio wavelengths[4-6], at optical wavelengths (J. T. Delaney, B. Lawless and G. A. Baird, unpublished) and in the X-ray band[7,8], but so far without success. Here we describe the results of a new experiment to correlate radio pulses at 858 MHz with events observed by Weber, but to a better radio sensitivity than has been achieved so far. The results are inconclusive at present, but there is strong evidence for the existence of discrete radio pulses of extra-terrestrial origin.

We used a 60-foot telescope operating at 858 MHz. To reduce spurious instrumental effects, we used a receiver of the correlation type in which the signal from the antenna is split between two identical channels, the outputs being multiplied together and then displayed on an analogue recorder. The
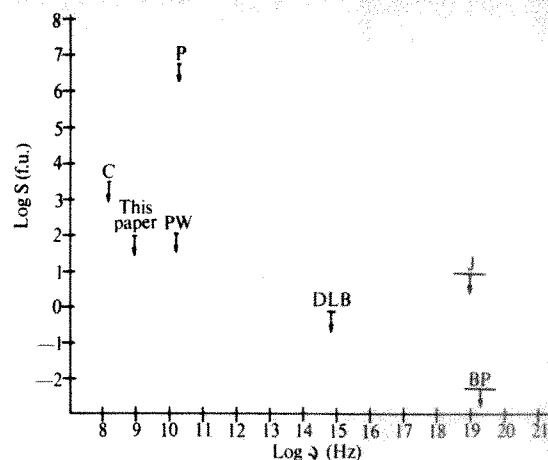
Fig. 1 Pulse detection limits achieved by various observers. C, Charman et al.[4]; P, Partridge[5]; PW, Partridge and Wrixon[6]; DLB, Delaney, Lawless and Baird (unpublished); J, Jelley[7]; BP, Baird and Pomerantz[8].

effective time constant at the output was about 1 s. Overall sensitivity was determined from observation of the Crab Nebula, assumed to have a flux density of 1,062 f.u. at 858 MHz. The r.m.s. noise level at the output, σ_N, corresponded to a signal received in the direction of the antenna maximum of 14 f.u. The half-power beamwidth of the antenna was 1.4 arc deg and approximated in angular size the extended regions of radio, X-ray and infrared emission at the Galactic centre. The minimum detectable level for pulses was $6\sigma_N$ at the recorder, corresponding to a received signal of 85 f.u. This sensitivity is compared with that of previous observers in Fig. 1.

Because the amplitude of possible pulses is not known the direction of origin of the source could be inside a cone with dimensions many times that of the beamwidth of the telescope. To improve angular resolution, we took a series of drift scans at constant declination, and attempted to correlate positional distribution of the pulses with the beamwidth. The area of sky scanned was approximately 1.4×4.4 arc deg[7], centred on Sgr A. Each scan took 20 min, and up to eleven such scans could be obtained each day.

A radio event was defined as a pulse which occurred during a useful observing session—one that was interference free and showed no receiver drifts, with pulse amplitude at least equal to six times the r.m.s. output fluctuation, and pulse duration not much greater than the recorder time-constant of 1 s. Fig. 2 shows an example of such an isolated event; the increase in level due to radiation from the region of the Galactic centre is also seen. Local interference and lightning discharges were observed on a number of occasions and necessitated the rejection of approximately 40% of the total data.

During June to December 1971, 804 useful drift scans were obtained giving a total of 270 h of observation. 97 events were noted, a mean reception rate of 0.36 events h^{-1}. The maximum amplitude was $30\sigma_N$, and the smallest recorded was determined from the criterion of detectability, $6\sigma_N$. The mean
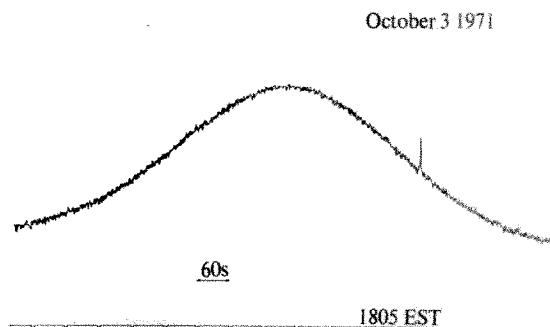
Fig. 2 Example of isolated pulse observed during drift scan of Galactic centre.
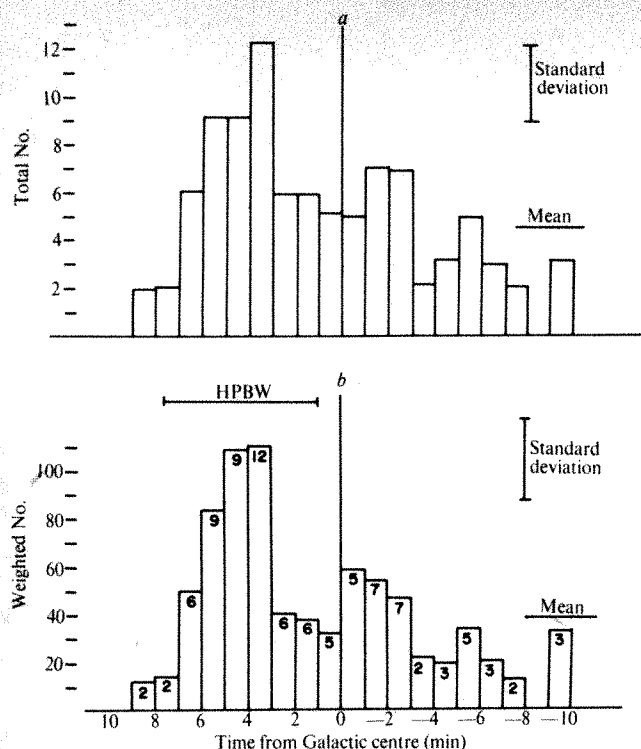
Fig. 3 Normalized distribution of radio pulses against time relative to continuum peak (*T*). *a*, Number of pulses; *b*, number of pulses weighted according to pulse amplitude.

amplitude was $9.7\sigma_N$ with a standard deviation $4.8\sigma_N$. As an initial check that the events were not due to weak interference from fixed terrestrial sources, the distribution with azimuth pointing of the antenna was first determined. A small increase in the distribution around azimuth 200° was noted, but was not statistically significant. We concluded that there was no significant dependence of event rate with azimuth.

For the first stage of the analysis, we attempted a correlation of radio events with the data on gravitational events supplied by Weber, though the latter were not complete for the period of our observations. But 222 gravitational events were recorded on 96 of the days, corresponding to a rate of 0.096 events h^{-1}. The number occurring during useful radio observing periods was 14; the expected number was 18.4. We examined the radio records at the times of the Weber events, but observed no radio feature of any kind within a period of ±5 min.

An analysis of the time interval between the radio and gravitational events was carried out for all events. Of the 21,534 time intervals, 103 occurred within the range ±1,000 min, and 9 occurred within ±60 min, in general agreement with the numbers expected if the events occurred independently and at random. The minimum time interval was 10.1 min and no significant grouping at any time interval was found. The expected delay of the radio events is 6 s, assuming that the gravitational waves travel undispersed with velocity *c* and the dispersion measure for radio waves propagating from the Galactic centre is 1,000 pc cm^{-3}. We therefore concluded that there was no significant correlation between gravitational events and the observed radio events. But coincidences could have been missed, because any one region of the Galactic centre was observed for only a fraction of the total time. The probability of a coincidence depends chiefly on the length of scan, the threshold level for detection and the amplitude probability distribution of the pulses. The latter is not known, but for pulses of amplitude $9.7\sigma_N$, on average only one in 7.5 would be observed; for those of amplitude $14.5\sigma_N$, corresponding to one standard deviation greater than the mean, the probability is one in 5.5. Also, for about a half-beamwidth at the ends of the scans (3.2 min), the probability is less by a factor of

about 2. Of the 14 gravitational events, an average of only 2 (±2) coincidences would be expected. So the results are not statistically significant, and in addition, the source of gravitational events could well lie outside the radio search area.

We also tried to determine the direction of origin of the events by measuring their time of occurrence relative to the peak of the continuum radiation from the Galactic centre (Fig. 2*a*). Fig. 3*b* shows a similar distribution, with the individual events weighted according to pulse amplitude; the numbers in the latter distribution refer to the number of events.

There is a slight trend towards an increase in number received from the direction of the Galactic centre (Fig. 3*a*), and an increase at about 3.5 min after transit. But if we take into account the amplitude of the pulses (Fig. 3*b*), it seems that there is a significant increase between +3 and +6 min. The peak corresponds to an increase of 2.4 s.d. over the mean, the probability of this occurring by chance being about 2%. Because the adjacent bin is of comparable amplitude, the probability of the two occurring together by chance is less than 0.1%. A change in the width of the bins does not seriously affect the statistics, but if the three bins between +3 and +6 min are not used in the determination of the mean and s.d., the significance of the amplitude of the largest is about five times the new s.d. There seems to be little difference in the two distributions, apart from the increase in the weighted number histogram, so we conclude that there might be a discrete source which is giving consistently larger pulses than average, for the region scanned.

We estimate the coordinates of this source to be:

RA = 17 h 48.2 min ± 1.3 min   Dec = − 28° 58′ ± 52′ (1950.0)

and the coordinates of the peak in the continuum emission are:

RA = 17 h 43.8 min ± 0.8 min   Dec = − 28° 58′ ± 10′ (1950.0)

The half-power beamwidth of the telescope seems to be larger in RA than the extent of the source (Fig. 3*b*). But this is consistent with a cutoff applied to the amplitude of the events. For a mean amplitude of pulses from the source of $9.7\sigma_N$, the apparent half-width of the source would be reduced from 6.4 min in RA to 3.5 min.

Some observations were also made in the direction of other sources and also at the same azimuths as those used for Galactic centre observations, though not for the same length of time. In 22 h observing, only one pulse occurred. We conclude that in the direction of the Galactic centre there are sources which emit pulses of radio waves of duration less than 1 s (as determined by the output time constant of the recording equipment) and a source which seems to contribute about 24% of the events, with pulses of consistently greater amplitude than the average of all events.

How do these events relate to known radio, optical, infrared, X-ray and γ-ray sources? Fig. 4 shows the scan region superimposed on a 5 GHz radio contour map[9], with the positions of 100 μm infrared sources[10], Uhuru sources[11], and PSR 1749–28 (ref. 12). The latter, within $0.35 ± 0.29$ arc deg in RA and 0.87 arc deg in declination from the possible discrete source, could be generating super pulses. If so, they would be of amplitude $\sim 10\sigma$ which, with the recorder time constant of 1 s and correction for the position of the pulsar in the telescope beam, gives an individual pulse energy of 4.0×10^{-21} erg cm^{-2} Hz^{-1}. The mean energy spectrum for the Crab pulsar, which has similar dispersion measure and may be at a similar distance, is[13] $\int I \, dt = 4 \times 10^{-22} (\nu/100)^{-1.9}$ erg cm^{-2} Hz^{-1}, a factor of about 600 less than the intensity of the observed pulses. But at 146 MHz giant individual pulses from the Crab of energy 600 times greater than the mean are observed at a rate of about one per day[14]. The estimated pulse rate from the source is about 0.5 h^{-1}, when corrections for the method of observation have been applied. But because of the small amount of information available on super pulses from other pulsars, a direct comparison is probably not significant. It is likely that PSR 1749–28 (equivalent age $P/\dot{P} = 2 \times 10^6$ yr) is considerably older than the Crab pulsar (2.5×10^3 yr, ref. 15).

Further, though the dispersion measures for both pulsars have similar values, it is likely that the mean interstellar electron density is appreciably greater in directions towards the Galactic centre than in directions towards the anti-centre. Cavallo and Ventura[16] give a distance of 366 pc for PSR 1749-28 in comparison with 1,527 pc for the Crab from an analysis of their periodicity-luminosity relationship. This implies that any giant pulses produced by PSR 1749-28 are at least an order of magnitude smaller than those produced by the Crab pulsar.

The possibility remains that most of the other events could also be produced by pulsars and hence could be related to supernova remnants in the Galactic centre region. The Crab pulsar was first detected from observations of giant pulses and is one of the few associations of a pulsar with a supernova remnant. Of the nearly 80 pulsars known at present, the only other two associations are in the constellations Vela[17] and Crux[18] and with IC 443 (ref. 18a). A number of supernova remnants exist in the direction of the Galactic centre (Fig. 4 and refs. 19, 20).

We find no correlations between the times of occurrence of the radio events and those of solar radio bursts, solar flares and sudden ionospheric disturbances.

Some of the radio events may be due to electromagnetic radiation from extensive air showers produced by cosmic rays (refs. 21, 22). The intensity at high frequencies of such a shower is proportional to $\cos^6 Z$ where Z is the zenith angle[23], and has the rather steep spectral index of 2. Because the maximum radio flux for showers occurring at the zenith at 520 MHz is about 10^5 f.u. for a minimum zenith angle at 74° the expected amplitude at 858 MHz is 16 f.u., less than 20% of the detectable level. The more recent results by Charman[24] at 500 MHz confirm this estimate.

Other interesting speculations are that the events might be associated with black holes, and produced either by charged particles falling into them[25,26] (which might also produce detectable gravitational radiation) or by the collision of black holes[27]. The discrete pulse source might then be produced by the former, but would require massive clouds of particles to fall into the black hole at the rate of about one every 10 h. The other events might also be produced in a similar way, but the collision mechanism, which would require one collision about every three hours, needs a rather large supply of black holes at the Galactic centre.

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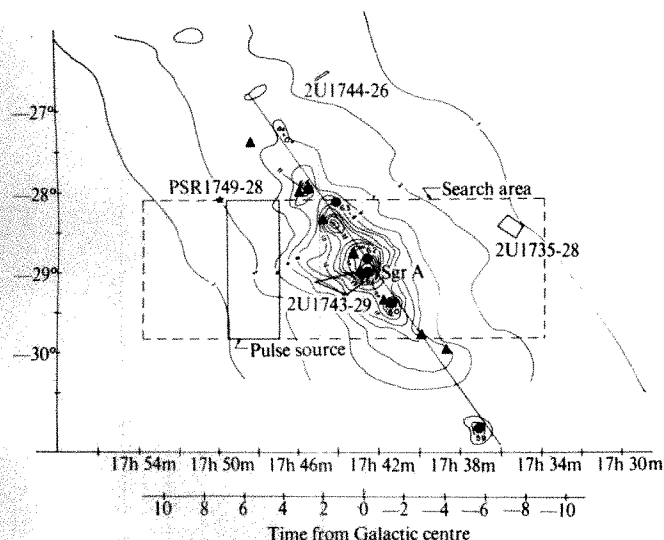
Fig. 4 Search area superimposed on 5 GHz radio contour map[9]. Also shown are Uhuru sources[11], PSR 1749-28 (ref. 12), 100 μm infrared sources (▲) (ref. 10) and non-thermal radio sources (●) (ref. 20).

5-μm Infrared Emission from Algol

DURING September 1972, we made a number of 5-μm observations of the eclipsing binary β Per (Algol) using the 60-inch infrared flux collector at Izana, Tenerife. Our photometer was of conventional design, having a nodding mirror to give sky background cancellation and using an indium antimonide detector cooled to 77 K. α Per was used as a comparison source and this in turn was calibrated against better known infrared standards such as α Lyr. Poor weather conditions did not allow us to make as many observations as we would have liked, but sufficient to define the principal light curve.

Fig. 1 shows our experimental results: the infrared light curve has been drawn on the assumption that it is symmetrical about both the primary and secondary minima. The principal source of error was vibration of the telescope in high winds. The Algol system is thought[1] to consist of three components: A—a main-sequence B8 star ($M_{bol} = -0.4$, log $T_e = 4.03$); B—a K0 subgiant ($M_{bol} = +3.1$, log $T_e = 3.66$); C—a main-sequence A5 star ($M_{bol} = +2.3$, log $T_e = 3.92$). This gives a total apparent M magnitude of +2.86.
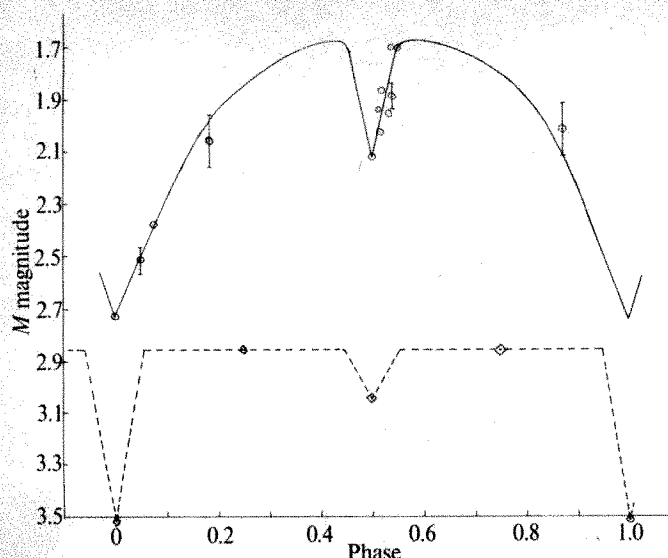
Fig. 1 Observations of Algol at 5 μm. ——, Infrared light curve; - - -, total intensity of the system, assuming that the component stars behave like black bodies.

There is clearly an infrared excess of 1.2 mag. The shape of the infrared light curve indicates that this infrared emission cannot be from the stars A and B; if it were, the infrared light curve would have the same shape as the optical light curve (dotted curve).

Chen[2] has observed Algol at 1.6 μm and found that the form of the infrared variation at that wavelength is similar to the optical variation. Thus whatever is causing the infrared excess at 5 μm should not cause an appreciable excess at 1.6 μm. This rules out an explanation in terms of a dust shell around the two stars, because the dust must have a temperature of less than 600 K for it not to radiate at 1.6 μm. This, in turn, suggests that the dust must be at distances greater than 300 $R_\odot$ from star A. A and B are separated by only 15.7 $R_\odot$, so that a dust shell of radius 300 $R_\odot$ or more could not provide any form of infrared eclipse.

The infrared excess can, however, be explained by free-free emission from an ionized hydrogen plasma cloud. Because we have observations at only one wavelength, we cannot provide a definitive model. A cloud of radius 15 $R_\odot$, temperature 10,000 K and electron density 10^9 cm^{-3} would radiate the required 5 μm flux. Such a cloud would be optically thin at infrared and visible wavelengths, but would become optically thick at about $\lambda = 5$ mm. It would not emit detectable fluxes of either radio or visible continuum radiation, nor would it emit detectable line emission (for example, H$_\alpha$). If the cloud has a temperature of 100,000 K the electron density can be slightly less, and the cloud does not become optically thick until $\lambda = 1.5$ cm.

Algol is a radio flare star whose spectrum rises at shorter wavelengths[3,4]. It has been observed at wavelengths of 11.1 cm, 3.7 cm and 2.8 cm, agreeing reasonably with the optical density we have estimated for the cloud at radio wavelengths. (The radio emission—thought to be synchrotron in origin—may have to pass through at least some of the cloud.)

Because the cloud must be optically thin at 5 μm, only stars A and B can produce the eclipses. The infrared excesses at primary minimum, secondary minimum and at maximum are in the ratios 1 : 2 : 4.5. It seems difficult to explain these figures if the gas cloud fills the Roche lobes, or orbits either or both of the stars. We conclude that most of the cloud must lie between the two stars. Thus the cloud will be smaller and slightly denser than we have suggested above. Finally, we emphasize that the curve shown is the best fit to our data but for any eclipsing system the intensity maximum would be expected at 0.25 phase.

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Radio Source Counts in Cosmology

SCHMIDT[1] has objected to an argument given in my 1968 Bakerian Lecture[2]. Fig. 2 of Kellermann's recent Warner Prize Lecture[3] shows combined differential source counts at 75, 20, 11 and 6 cm. The points show a Euclidean distribution for values of the integral count between ~ 10 and $\sim 10^3$ sources sr^{-1}. Above 10^3 sources sr^{-1} the counts deviate from a Euclidean distribution in the way that is expected for cosmologically distant objects, but for less than 10 sources sr^{-1} the counts deviate from Euclidean in a reversed sense. This so-called "steep" part of the distribution therefore involves only ~ 100 sources over the whole sky. The point from my Bakerian Lecture, now under criticism, was that the latter deviation can be regarded as a local fluctuation in which ~ 5 nearby sources sr^{-1} are considered to be missing at the high flux end of the source distribution. The data from four surveys, given in the reference cited above, strongly support this position.

The Euclidean behaviour for source counts between 10 and 10^3 sr^{-1} can be understood on the basis that the sources in question are not at significant cosmological distances. This explanation can be used either for the steady state model or for non-evolving Friedmann models. The opposite point of
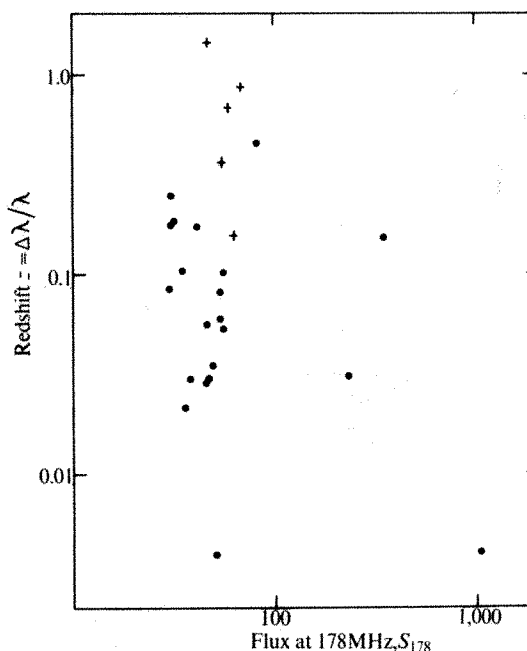
Fig. 1 Plot of redshift z against flux at 178 MHz, S_{178}, for the 26 sources of the 3 CR catalogue with $S_{178} > 30 \times 10^{-26}$ W m^{-2} Hz^{-1}. +, QSO; ●, radio galaxy.

view, that the distances are of cosmological order, leads to the first of the four curious coincidences discussed by Kellermann[3].

By adding optical data it would be possible to carry the argument further. Redshifts are not available, however, for more than a small fraction of the sources. The data discussed by Schmidt concern only 26 very high-flux sources. The redshifts z of these sources, plotted against the 178 MHz flux S_{178}, are shown in Fig. 1. The absence of a significant correlation between redshifts and fluxes can be interpreted in two ways: the optical redshifts are not distance indicators, or the 26 sources in question constitute a fluctuation.

In the first case, issues striking at the root of our most cherished cosmological beliefs would be involved. In the second case it is meaningless to attempt to base far reaching cosmological conclusions on a very small sample of 26 sources constituting only a fluctuation.

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Fig. 1 Locations of the transmitter at Malvern and receivers at Chilbolton, Aberystwyth and Wardle. The angle between magnetic north and the Malvern-Wardle line, actually only 1°, is slightly exaggerated for clarity.

Reply to Hoyle

HOYLE'S assertion that only 5 sources per steradian are missing at the bright end[1] is based on the apparent Euclidean nature of the source counts. My derivation of the steady-state source counts[2] expected if radio galaxies have cosmological redshifts shows that the Euclidean slope of -1.5 is not reproduced at the count levels of interest.

The large scatter in the diagram of redshift versus radio flux density shown by Hoyle[1] is usually interpreted as caused by the large range of absolute radio luminosities—an interpretation not mentioned by Hoyle. The tight correlation between the redshift and the optical flux density of radio galaxies[3] is quite similar to that observed for the brightest galaxy in clusters of galaxies[4]. There is at present no attractive alternative to the conclusion (or, in Hoyle's words, the cherished cosmological belief) that in both cases the tight correlation is caused by a velocity-distance relation and hence that the redshifts are cosmological.

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Multistatic Incoherent Scatter Measurements of Ionospheric Drift Velocity

THE observed behaviour of the ionospheric F-region has proved difficult to understand, and one of the principal difficulties has been that, until recently, there was little reliable information about the true plasma drift velocities. Apparent horizontal drift speeds have been measured for many years by means of the "fading" method[1]: interpretation of data from these experiments is complex[2], and it is now clear that the results give only the drift of large electron density irregularities which, although of considerable interest in itself, is not necessarily the same as the drift of the plasma as a whole. Plasma velocity measurements have been made by plotting the movements of luminous chemical tracers released in the ionosphere from rockets or gun launched projectiles[3,4]. Information from this type of experiment is of good quality, but is necessarily limited in quantity. An alternative technique is incoherent scatter radar, which measures the doppler shift of the scattered signal and determines one component of the ion drift velocity; the advantages of this method are that measurements can be pursued systematically as functions of time over a wide range of heights and that systematic errors can be minimized by careful equipment design. Incoherent scatter drift measurements were first made by Carru et al.[5], who measured one component of the velocity, aligned nearly parallel to the direction of the geomagnetic field. A large body of similar measurements from the French installation now exists, and has been used to study thermospheric dynamics[6]. The incoherent scatter radar at Jicamarca, Peru, has measured the field perpendicular component near the magnetic equator[7], and the vertical component has been measured by the Millstone Hill radar in Massachusetts[8].

The field aligned component of ion drift is attributable to plasma diffusion and neutral air winds; above 150 km, the field perpendicular component is due only to electrostatic fields. It is therefore desirable to measure all components of drift velocity. Some work has been reported in which a steerable monostatic radar has been pointed obliquely in several directions successively, so as to measure more than one velocity component. Thus Evans[9] has determined both horizontal components of the velocity vector and Harper[10] has been able to measure all three orthogonal components. These measurements are necessarily made at different points in the ionosphere at different times, and while the mid-latitude ionosphere generally varies sufficiently slowly in space and time that the measurements can be treated as coincident, it would be more satisfactory to make measurements simultaneously in the same scattering volume. We present here multi-component incoherent scatter drift measurements which are coincident in space and time; these were achieved by receiving the scattered signals at more than one site.
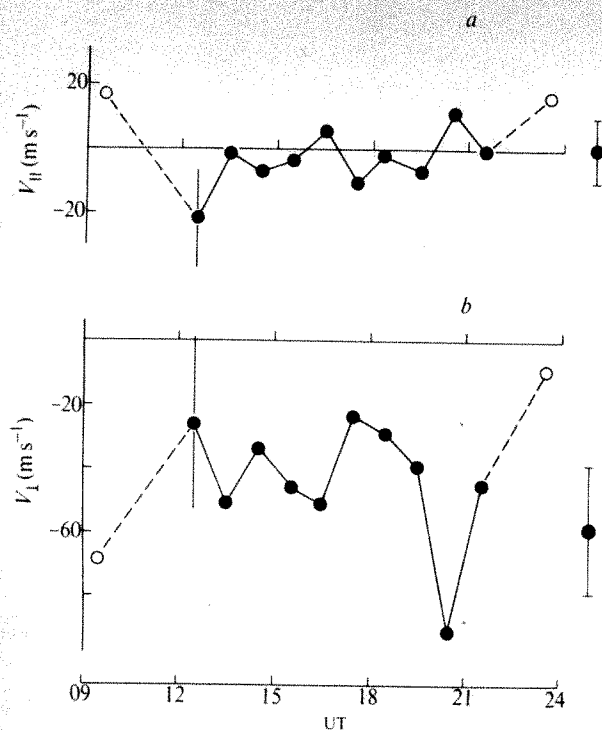
Fig. 2 Hourly averages of $V_{||}$ (positive upwards) and $V_\perp$ (positive northwards) at 270 km height above Malvern on April 17, 1972, calculated from Chilbolton and Wardle data. Open circles represent uncertain values. The vertical bars show typical errors, ± 10 m s^{-1} for $V_{||}$ and ± 20 m s^{-1} for $V_\perp$.

The equipment is situated at four sites and is an extension of the high power pulsed radar described previously[11]. The transmitter is at Malvern (52.1° N, 2.3° W) and uses a 43 m diameter vertically pointing circular paraboloid to transmit a continuous wave of 40 kW mean power at a radio frequency of 400.50 MHz. The three receiving sites are at Chilbolton (51.1° N, 1.4° W), Jodrell Bank (Wardle, 53.1° N, 2.6° W) and Aberystwyth (Capel Dewi, 52.4° N, 4.0° W): their distances from Malvern are 126 km, 110 km and 115 km respectively at well separated azimuths (Fig. 1). The aerial at Chilbolton is a 25 m diameter circular paraboloid[12], and that at Wardle a 25×36 m elliptical paraboloid[13], both fully steerable. The Aberystwyth aerial consists at present of two 12×25 m parabolic cylinders, connected to form a single aperture, movable in elevation. These three aerials receive signals incoherently scattered from the plasma in a scattering volume vertically above Malvern. The height h of the scattering volume is selected by pointing the receiving aerials at appropriate elevation angles, and the height resolution Δh depends on the beamwidth of these aerials (about 2°), being about 13 km in the E layer at $h = 120$ km and 40 km in the F2 layer at $h = 275$ km.

The signal characteristics measured are the signal-to-noise power ratio and the spectral distribution of signal power. At each receiving station, the 50 kHz intermediate frequency signal is clipped and recorded on magnetic tape as one-bit samples of the waveform. The tapes are later played back, using a 210 channel correlator which computes the autocorrelation function, integrating over a suitable period. A digital computer is used to transform the autocorrelation function into the corresponding power spectrum, and a best fitting theoretical spectrum determined[14], yielding as parameters the electron and ion temperatures, T_e and T_i, and one component of drift velocity, V_m. We define V_m as positive when it is directed upwards. By the use of a pure c.w. transmitted signal, instrumental distortions of the spectra are minimized, and good fits between observed and calculated spectra can be obtained. Thus, unreliable spectra (for example, those contaminated by r.f. interference) can be eliminated readily by inspection. The errors of measurement by day, with good signal strength and about 20 min integration, are ± 15 K for

T_e and T_i and about ± 12 m s^{-1} for V_m. During the winter night the temperature error increases to about ± 100 K and the velocity error to about ± 70 m s^{-1}; the velocity data are then not accurate enough to be useful. In contrast, the possible systematic error due to frequency instabilities in the system (less than 1 part in 10[8]) is only about ± 1 m s^{-1}. The temperatures determined simultaneously at two or three receiving sites nearly always agree within their estimated errors, as expected.

To date, most of the observations have been made at Chilbolton and Wardle only. Measurements at two stations simultaneously do not suffice to determine the velocity vector completely, but only its projection on a certain plane. In the case of Chilbolton and Wardle, it is a reasonable approximation to assume this plane to be that of the magnetic meridian, which is inclined to the Chilbolton–Malvern line by only 20° and to the Malvern–Wardle line by only 1° (Fig. 1). If this approximation is made, the velocities V_m measured at the two stations can be combined to give the field-aligned component of drift, $V_{||}$, and the perpendicular component, $V_\perp$, in the meridian plane. The approximation fails if the drift velocity in the magnetic east–west direction is very much larger than that in the meridian plane, but it seems most unlikely that this will be the case generally. It so happens that the directions of the measured values of V_m make rather small angles with the magnetic field (1°–15° for Wardle and 30°–45° for Chilbolton, depending on height) and in consequence $V_{||}$ is more accurately determined than $V_\perp$.

Fig. 2 shows values of $V_{||}$ and $V_\perp$ (plotted as hourly averages) at 270 km height on a magnetically undisturbed day, April 17, 1972. $V_{||}$ varies slowly with time and is not greater than 20 m s^{-1}, the fluctuations probably being statistical. On this day $V_\perp$ exceeded $V_{||}$ in magnitude and was directed consistently
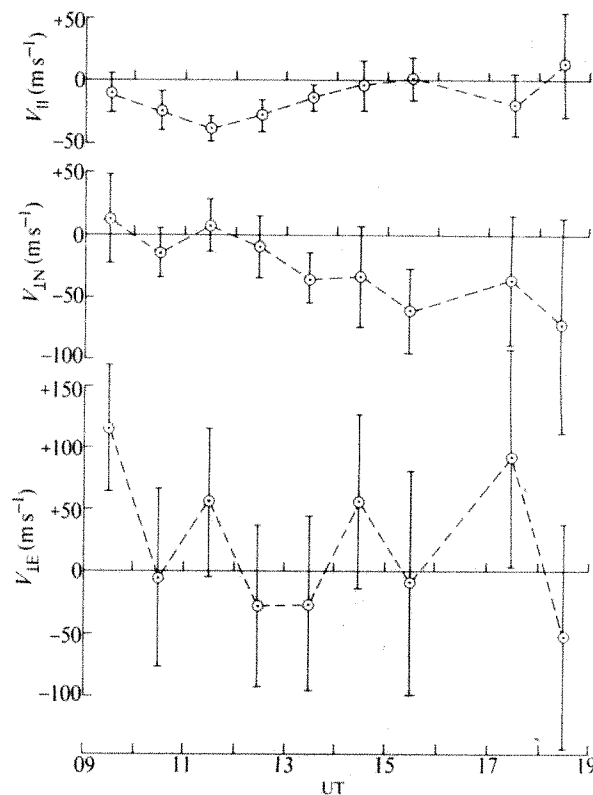
Fig. 3 Drift velocities at 270 km height deduced from simultaneous measurements at Chilbolton, Aberystwyth and Wardle. The component parallel to the geomagnetic field is $V_{||}$, reckoned positive upwards; the components perpendicular to the geomagnetic field are $V_{\perp N}$ (in the magnetic meridian, positive northwards) and $V_{\perp E}$ (in the magnetic eastward direction). Data obtained on November 15 and November 16, 1972, have been averaged.

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southward from 1230 to 2130 UT at least, and probably for longer. On this day at least $V_\perp$ was opposite in direction to the theoretically calculated Sq drift, which is poleward during the day at middle latitudes[15]. But the diurnal variations of $V_\parallel$ and $V_\perp$ observed on other days are different, particularly when magnetic activity is present, and we cannot say yet whether the values in Fig. 2 are typical even of quiet days. Fig. 3 shows drift velocity components deduced from simultaneous measurements at all three receiving sites; further measurements of this type are being made, and will be presented later.

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Location of the Proto-Atlantic Suture in the British Isles

WILSON[1] postulated, using faunal, tectonic and stratigraphic evidence, that the northern and southern parts of the British Isles were once separated by an ocean (the proto-Atlantic Ocean) which has since been destroyed by a continental drifting process in which the British Isles resulted from the welding together of land masses originally on different sides of the ocean. Following the stimulus of Wilson's idea and the possibility of plate tectonic theory providing an explanation for the continental movements, the geology of the central British Isles has been reappraised[2-7] and the igneous, structural and stratigraphic features of the area have been related to the motion of lithospheric plates being thrust under continental masses as the continents converged.

Dewey and Pankhurst[4] postulate that a plate thrust northwards under the Scottish Highlands is consistent with the orogenic features of the area. Fitton and Hughes[7] have shown from petrochemical analyses that the regional variation in magma type in the Ordovician volcanic rocks of England is consistent with what would be produced by a plate being thrust
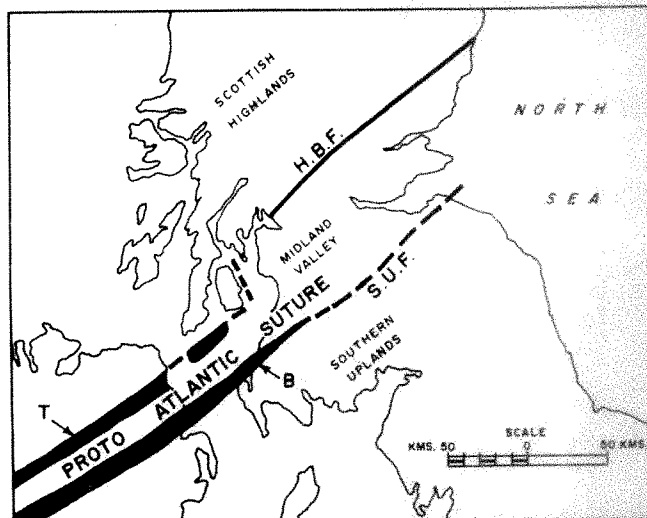
Fig. 1 Suggested location of the Proto-Atlantic Suture in Scotland and Northern Ireland. Black areas are ophiolitic rocks, known and deduced from geophysics. Dashed lines are faults, known and deduced from geophysics. HBF, Highland Boundary Fault; SUF, Southern Uplands Fault; B, Ballantrae Ophiolite Complex; T, Tyrone Igneous Complex. I believe there has been a tear in the oceanic plate along the line of Arran causing the offset of the line of ophiolites. I have interpreted a magnetic anomaly in the North Channel (shown as the isolated black area west of Arran) as an isolated wedge of ophiolites on the continuation of the Irish zone. There is no magnetic evidence to indicate any fault along the traditional line of the Highland Boundary Fault (just south of the Mull of Kintyre). The Tertiary igneous centre of Arran could well have been located by this tear in the lithospheric plate.

southwards. Although the diverging plate model appears reasonable there is an inconsistency because both models position their subduction zones along the line of the Southern Uplands fault where the ophiolitic rocks at Ballantrae are thought to be fragments of oceanic crust emplaced during the underthrusting.

In these models the Southern Uplands are considered to overlie oceanic crust compressed between two continental masses[2-6]; however, the geophysical evidence reviewed by Powell[8] indicates that the Southern Uplands are underlain by a crust of normal continental thickness (30 km) and that thickening by compression from an oceanic crust (average thickness 7 km) is unreasonable. The estimates of Agger and Carpenter[9] confirm the results described by Powell.

Another problem with considering the Southern Uplands as overlying oceanic crust is that andesitic volcanics (of Caradocian age) occur at Bail Hill near Sanquar within the Southern Uplands[10]. Dewey[3] admits that andesitic rocks would not be expected over an area of oceanic crust and postulates their present position to be the result of a moving seafloor. It is difficult to imagine this happening because according to Dewey's model the andesites occur between two plates being underthrust in different directions away from the andesites.

Compilations of gravity data in the area[11-14] show that there is no gravity high over the Southern Uplands as would be expected over a thin crust or a crust formed of dense basic material. The Midland Valley, however, does coincide[13] with a large regional gravity high and this feature has induced me to consider the evidence that the Midland Valley may mark the proto-Atlantic suture.

The Midland Valley[13] consists of a graben flanked by the Southern Uplands fault and the Highland Boundary fault and associated with each of these faults is a zone of ophiolitic rocks. The assemblage of black shales, cherts, spilites, gabbros and serpentinized peridotites of the Ballantrae Complex[16] can be traced, using aeromagnetic data[17], across into Northern Ireland (Fig. 1). A similar assemblage of rocks occurs in a thin zone along the Highland Boundary in Scotland[18] and these rocks seem, on the basis of published gravity[19] and aeromag-

netic[17] data, to correlate with the ophiolitic Tyrone Igneous Complex[12] of Northern Ireland.

The absence of blue schists along the Highland Border region does not necessarily mean that this is not a subduction zone because the mode of emplacement of the ophiolites may have occurred without high pressure effects, for example they may have been detached from the lithospheric plate as a single slice of material.

It must be admitted that the position of this zone is not definite under the North Channel and there is the possibility of a north-south displacement in the vicinity of Arran. Because ophiolites are now believed to be fragments of oceanic crust emplaced by thrusting, welding and scraping along the zones where mobile oceanic crust underthrusts continental crust[20], the two zones of ophiolites flanking the Midland Valley are likely to mark two subduction zones. I thus consider the Midland Valley to be the oceanic remnant of the proto-Atlantic Ocean. This model means that the Highland Boundary fault and the Southern Uplands fault mark the positions of diverging Benioff zones and that the Midland Valley consists of a basement of oceanic origin overlain by sediments eroded from the flanking continental areas.

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Couple on a Bar Magnet

Whitworth and Stopes-Roe[1] have described experiments in which the couple on a bar magnet was measured with and without the magnet being immersed in a paramagnetic fluid, and have interpreted their results as supporting the Kennelly formulation in which the couple on a magnet is proportional to H rather than the Sommerfeld formulation which makes it proportional to B. But they add that they expect the couple on a magnet immersed in a medium to depend on its shape. Their experiments refer to long thin magnets, which they regard as true magnetic dipoles, and the Sommerfeld equations would be correct for magnetic shells or current loops.

If we accept these statements and wish to generalize the equations to cover magnets of any shape, the torque equations

must include a shape factor. Thus in the Kennelly system, the couple **T** on a magnet of moment **j** could be written

$$T = S_k \, \mathbf{j} \times \mathbf{H} \tag{1}$$

In the Sommerfeld system with moment m

$$T = S_s \, \mathbf{m} \times \mathbf{B} \tag{2}$$

To agree with Whitworth and Stopes-Roe the Kennelly shape factor S_k must be 1 for a long thin magnet and μ_r for a magnetic shell, and the Sommerfeld shape factor S_s must be 1 for a shell and $1/\mu_r$ for a long thin magnet; μ_r is the relative permeability of the medium.

I accept Whitworth and Stopes-Roe's experimental results and think their suggestion of a shape effect is probably correct. I disagree with their preference for long thin magnets, and would choose spheres, cubes or cylinders with equal lengths and diameters. Such shapes would not pre-empt the results in favour of either the Kennelly or Sommerfeld system. They also approximate best to ideal dipoles in the sense that the external field they produce conforms closely to the inverse cube law for dipoles.

The shape factor has been calculated by Smythe[2] for a sphere in a permeable medium. His derivation is preceded by the statement that a permanent magnet has the same permeability μ_v as free space, and inserting a body of this permeability in a medium of permeability μ distorts the field at its boundaries. This distortion is due to inserting a vacuum into the medium and is quite independent of the actual magnetization of the magnet.

The equation derived by Smythe for the torque is

$$T = \frac{4\pi\mu_v \, a^3 \, MB \sin \alpha}{2\mu + \mu_v} \tag{3}$$

where a = radius and M = magnetization of the sphere in A m^{-1}.

If I introduce the relative permeability of the medium μ_r, equate $4\pi a^3 M/3$ to the Sommerfeld moment and use vector notation, equation (2) becomes

$$T = \mathbf{m} \times \mathbf{B} \frac{3}{2\mu_r + 1} \tag{4}$$

Substituting $\mathbf{m} = \mathbf{j}/\mu_v$ and $\mathbf{B} = \mu_r\mu_v\mathbf{H}$ gives the equivalent Kennelly form

$$T = \mathbf{j} \times \mathbf{H} \frac{3\mu_r}{2\mu_r + 1} \tag{5}$$

Thus the shape factor for the sphere is $3/(2\mu_r + 1)$ in the Sommerfeld system and $3\mu_r/(2\mu_r + 1)$ for the Kennelly system. If shape factors are ignored, an experiment similar to that of Whitworth and Stopes-Roe carried out on magnets that are neither long bars nor thin disks would seem to disprove both systems.

Some people prefer to avoid these shape factors by saying that immersing the magnet in a medium changes its moment. They are quite entitled to this point of view. It implies that equation (1) or (2) without shape factors does not predict the torque but defines a new concept, "the magnetic moment of a magnet in a medium". No further use can be made of this moment without calculating the shape factor that relates it to the moment in free space. The present standpoint that the magnetic moment of a uniformly and permanently magnetized body is unchanged by surrounding it by a magnetic medium is equally valid and in my opinion somewhat more convenient. Of course, a non-uniformly magnetized body in a non-uniform field presents additional problems and it is probably not meaningful to speak of its moment.

With the correct use of shape factors either the Kennelly or Sommerfeld system can be used. If, however, shape factors

are necessary to predict the torque on a permanent magnet, should not the question of forces on a current-carrying conductor immersed in a magnetic medium be re-examined? Consider as an example a thin film-shaped conductor immersed in a medium of relative permeability μ_r. The permeability of the conductor is identical with that of a vacuum just as Smythe assumed for a magnet and both B and H are parallel to the plane of the film. It is certain that H in the film is precisely the same as H in the medium and, also, for an experiment similar to that of Whitworth and Stopes-Roe, neglecting the self-demagnetizing field of the tank, it is the same as if the paramagnetic liquid were removed. B in the conductor is also the same as if the liquid were removed. If the electric current is due to electrons moving in a medium with the same permeability as free space, it is difficult to avoid the conclusion that the force on these electrons is not affected by surrounding the conductor with a magnetic medium.

If, however, the plane of the conductor is turned so that it is normal to the field, both B and H within the conductor are increased. To assume, however, that the force depends on the orientation of the conductor leads to difficulties—two current-carrying conductors should experience equal and opposite forces. There seem to be two possible solutions to this paradox. One is to suppose that the force on a conductor whatever its orientation is unaffected by a surrounding medium. This could be justified by saying that any change in B or H when the medium is introduced arises from unanchored fluid molecules incapable of exerting a force on the conductor. An alternative suggestion was made during a discussion on this subject at the June 1972 meeting of the Magnetism Group of the Institute of Physics in Oxford. According to this suggestion part of the force on the conductor may arise from a hydrostatic pressure gradient in the fluid. Such a force might vindicate the generally accepted assumption that the force on a current-carrying conductor is proportional to B.

Whitworth and Stopes-Roe have shown that these questions can be investigated experimentally, and more experiments are clearly desirable. In general in such experiments, the self-demagnetizing field of the tank may need to be considered, although Whitworth and Stopes-Roe seem to have eliminated this factor with their particular arrangement.

I thank Dr F. J. Lowes for comments and for drawing my attention to ref. 2.

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Preparation of Tritium-labelled Talc

TALC, a native hydrous magnesium silicate approximating to the general formula $Mg_3Si_4O_{10}(OH)_2$, is extensively used in industry in addition to its wide acceptance as a cosmetic and toiletries product. Although chemically inert, it produces a number of biological effects including tissue granulomata[1,2] and a form of pneumoconiosis after inhalation[3,4]. A recent report[5] suggesting an association of cancer of the cervix and ovaries with the presence of talc particles at these sites has caused disquiet about its safety in use. Although the evidence is equivocal, it follows the acceptance of a causal relationship between exposure to asbestos dust and mesothelioma[6].

The detection of talc particles in tissues, essential for the elucidation of the mechanisms of pathogenicity, presents considerable difficulties. Although the extraction replication technique developed by Henderson *et al.*[7] offers an elegant

means for the identification of talc particles in tissues, the small areas that can be surveyed by electron microscopy do not provide an overall picture of particle distribution. Furthermore, the adventitious contamination of tissues during the preparation of specimens for examination cannot be ruled out. The value of using a suitably labelled radioactive talc for such studies is self-evident, and the use of tritium-labelled asbestos[8] has greatly facilitated the localization of asbestos fibres in tissues.

A method has now been developed for the preparation of tritium-labelled talc. The process involves two stages; first, the partial dehydration of talc under controlled conditions, and second, the rehydration of the material using tritiated water. The talc used conformed with the specifications of the British Pharmacopoeia 1968.

The partial dehydration of talc was effected by heating talc in a platinum dish at $835-840^\circ$ C for 1 h resulting in the loss of 1 molecule of H_2O. The study of the dehydration of kinetics of talc showed that below this temperature no loss of H_2O occurred, and that at temperatures in excess of 900° C the second molecule of H_2O was lost, gradually leading eventually to complete dehydration at $1,000^\circ$ C. The reincorporation of 1 molecule of H_2O into the partially dehydrated talc was achieved by refluxing the material with 50 volumes of benzene/water azeotropic mixture (92 : 8) for 2 h. The talc was filtered on a No. 4 sintered glass filter crucible and the last traces of solvents removed at 130° C under vacuum. Electron microscopy and X-ray diffraction studies showed that the rehydrated material was virtually identical with and indistinguishable from the original talc. It was found that talc could be repeatedly subjected to the processes of partial dehydration and rehydration, employing the methods described, without any substantial alteration in its physical properties or chemical composition.

The efficiency of the rehydration procedure was considerably improved by heating the partially dehydrated talc and 5 volumes of benzene/water azeotropic mixture contained in sealed ampoules in an autoclave at 15 pound inch^{-2} pressure for 30 min. The ampoules were opened, centrifuged at 3,000 r.p.m. for 5 min and the supernatant liquid decanted. The rehydrated talc was washed twice with distilled water, recentrifuged and finally dried at 130° C under vacuum. This procedure was adopted for the incorporation of tritiated water into talc, and the inclusion of tritiated water into the benzene/water mixture (0.5 mCi ml.$^{-1}$) resulted in the formation of tritium-labelled talc (15,000 d.p.m. mg^{-1}). The thermal stability of this labelled material was similar to that of the rehydrated talc and there was no evidence of exchange with H_2O at 100° C.

Biological investigations on the tissue distribution of the tritium-labelled talc are currently in progress.

We thank Mr J. K. Foreman for X-ray diffraction studies.

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BIOLOGICAL SCIENCES

A Unique RNA Species from Maturing Mouse Spermatozoa

STUDIES on ejaculated spermatozoa have shown that RNA is either absent or present only in trace amounts[1-4]. Work on RNA synthesis during spermatogenesis, however, suggested that RNA might be present in maturing spermatozoa. Although histochemical techniques disclosed little cytoplasmic RNA after the second meiotic division[5], Monesi's autoradiographic studies on mouse testes have demonstrated a small burst of post-meiotic nuclear RNA synthesis that declined upon spermatozoan maturation[6]. Moore has also shown active RNA polymerase in early spermatids[7]. Although RNA has not been quantitatively detected in ejaculated spermatozoa, incorporation of radioactive RNA precursors has been demonstrated[8] and we have extended these findings. Our studies on RNA metabolism in maturing mouse spermatozoa (from the epididymis and the ductus deferens) reveal the presence of larger amounts of RNA than previously reported for ejaculated spermatozoa. We have not investigated the RNA content of the ejaculated spermatozoa.

The epididymis and ductus deferens were dissected from mature random bred Swiss mice and placed in a small Petri dish. Spermatozoa were stripped from the ductus deferens, and the epididymides were chopped with a sharp razor blade. The chopped tissue was suspended in 4 ml./mouse of Beatty's media[9], swirled for 5 min and then strained through a wire screen (16 mesh) into a centrifuge tube. The sample was centrifuged at 10g for 30 s to pellet contaminating cells. The spermatozoa were transferred to a clean centrifuge tube, counted in a haemacytometer and centrifuged for 15 min at 600g. No contaminating cells (except for about 1%, RNA-free erythrocytes) were seen in the haemacytometer or in fixed smears.

The content of RNA in the sperm pellet was determined by the orcinol method[10]. RNA was extracted at 55° C with phenol and chloroform[11,12], treated with iodoacetate treated[13] beef pancreatic DNAase I (Worthington, electrophoretically pure), and extracted further with cold phenol and chloroform. The RNA sample was dissolved in an appropriate amount of 0.04 M Tris, 0.02 M sodium acetate, 0.001 M EDTA, 0.5% SDS at pH 7.8.

Table 1 RNA Content of Mouse Spermatozoa

Spermatozoa sample	pg RNA sperm (ribose determinations on whole sperm)	% Hydrolysed with RNAase	pg RNA sperm RNA extraction yields (OD 260)
Total sperm*	0.476±0.071	67.2±19	0.167±0.026
Caput epididymal sperm	0.648±0.083	—	0.260±0.012
Cauda epididymal sperm	0.236±0.030	—	0.091±0.007
Ductus deferens sperm	0.592±0.112	—	0.258±0.112

*Total sperm is a mixture of epididymal and ductus deferens spermatozoa and represents 26% from the ductus deferens, 50% from the cauda epididymis, and 24% from the caput epididymis (average haemacytometer counts).

Table 1 lists the RNA content of spermatozoa in the epididymides plus the ductus deferens, caput epididymis, cauda epididymis and ductus deferens. Total spermatozoa (from epididymis and ductus deferens) showed an average decrease of 67% upon pancreatic RNAase treatment (for 20 h at 37° C at pH 7.8) as determined by the ribose colorimetric assay[10].

The amount of purified RNA was determined from OD 260 measurements by using a value of 214 for $E_{1\%}^{1cm}$ at 260 nm in 0.1 M NaCl[14]. Colorimetric assay on whole spermatozoa and RNA extraction yields (OD 260) show a similar trend for differences among the spermatozoa from the caput and cauda epididymis and ductus deferens. The drop in RNA content in the older cauda epididymis spermatozoa with a later increase in ductus deferens spermatozoa appears to indicate that RNA synthesis is accelerated or re-initiated in the ductus deferens spermatozoa. Variable contamination has been excluded.
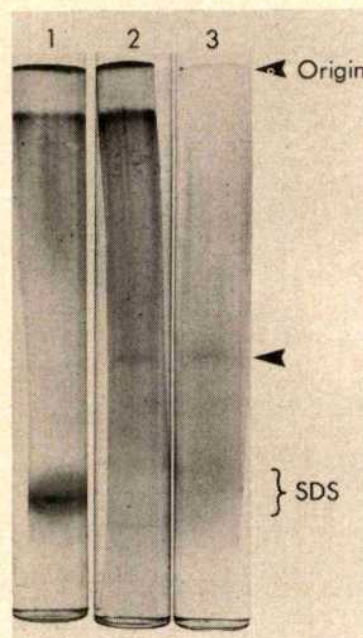
Fig. 1 Gel electrophoresis of purified epididymal and ductus deferens spermatozoa. RNA extraction was performed as described in the text, except at 40° C and with no DNAase treatment. The purified RNA was electrophoresed on polyacrylamide gels containing 2.4% acrylamide and 0.12% bisacrylamide. Gels were run at room temperature in a 0.04 M Tris, 0.02 M sodium acetate, 0.001 M EDTA buffer at pH 7.8 for 2 h at 5 mamp/gel. Gels were fixed for 15 min in 1 M acetic acid and stained for 1 h in 0.2% methylene blue. They were destained in distilled water. (1) Treated with pancreatic RNAase. (2) No enzymatic treatment. (3) Treated with pancreatic DNAase I.

Gel electrophoresis of the extracted RNA (Fig. 1) demonstrated the presence of an RNA band corresponding to a molecular weight of 190,000±5,000 daltons (about 11S). This molecular weight represents 16 different gels from 10 different sperm samples and was obtained by measuring the electrophoretic migration distance and from a semi-log plot of molecular weight against migration distance. DNAase treatment has no effect on the 11S band, whereas RNAase treatment removes the band. The band that was removed with DNAase treatment was seen routinely in non-DNAase treated RNA samples purified from other tissues (liver and fibroblasts); it is purple (as opposed to blue for RNA) when stained with methylene blue, and appears to represent DNA fragments. Gel analysis of sperm RNA from the caput and cauda epididymis and ductus deferens gave identical results. A small molecular weight RNA (3S to 4S) has been seen with gel electrophoresis and SDS sucrose gradients when the sperm RNA was extracted at 55° C. This 4S band was not detected when the RNA was extracted at 40° C.

The presence of this 190,000 dalton RNA in mouse spermatozoa might be explained by one of the following: (1) The RNA seen could *a priori* be the result of contaminating cellular material. This possibility is highly unlikely because the method of preparing spermatozoa resulted in no microscopically detectable contaminating cells and ribosomal RNA is not seen upon gel electrophoresis or sucrose gradient centrifugation.

(2) It may be a histone mRNA, biosynthesis of an arginine rich histone (protamine) has been observed during late spermatogenesis[6,15-17]. There is an increase in arginine and cystine and a decrease in other amino-acids as spermatozoa pass through the epididymis of the bull[16]. The 11S sperm RNA might be the message for this arginine rich histone. The electrophoretic migration (Fig. 1) corresponds to the migration seen for histone mRNA[18,19]. As there is no ribosomal RNA present, we must assume that active protein synthesis is not occurring during this maturational stage of spermatogenesis. If the 11S sperm RNA is a message it may be left over from earlier protein synthesis, and be resistant to whatever mechanism resulted in the degradation of the ribosomal RNA. (3) The mitochondria of the spermatozoa may be the source of the 11S RNA. Mitochondrial 11S RNA has been seen in sea urchin embryos[20]. Bands corresponding to the mitochondrial ribosomal RNA, however, were not seen for sperm RNA. (4) The 11S RNA may be the result of the RNA degradation which occurs naturally in the spermatozoa or as a result of the RNA extraction. Sheid has reported an unusual component in bull sperm that degrades RNA into non-dialysable fragments[21]. If the RNA is being degraded during the extraction, however, we would not expect to see the same sharp band from different samples and the migration patterns for all sperm RNA samples were identical. Also when sperm was extracted together with liver the electrophoretic pattern of the liver RNA was normal. (5) It may be a species of RNA or an RNA complex that is unique to sperm.

At present we are attempting to determine if sperm RNA is pre- or post-meiotic. Post-meiotic synthesis of RNA would indicate haploid gene expression, which must be postulated to explain *t*-allele segregation distortion of mice[22] and which could explain deficient fertilization of human diplo-Y spermatozoa[23].

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Fusion of Rat and Mouse Morulae and Formation of Chimaeric Blastocysts

THE induction of chimaerism by the aggregation of blastomeres of different mouse strains is one of the most remarkable recent contributions of experimental embryology[1,2].

Last year it was pointed out (Dr A. McLaren, private communication) that the possibility to fuse morulae of different species had not been sufficiently explored[3]. I therefore undertook a series of experiments to investigate whether aggregation of rat and mouse morulae can be induced, using basically the same techniques as those for aggregation of mouse morulae[3,4].

Mouse morulae (C3Hf × Swiss, 8–16 cell stage) were flushed from the utero-tubal region with culture medium on day 2 of pregnancy at 2100 h, day 0 of plug, 14 h of light, 10 h of dark-
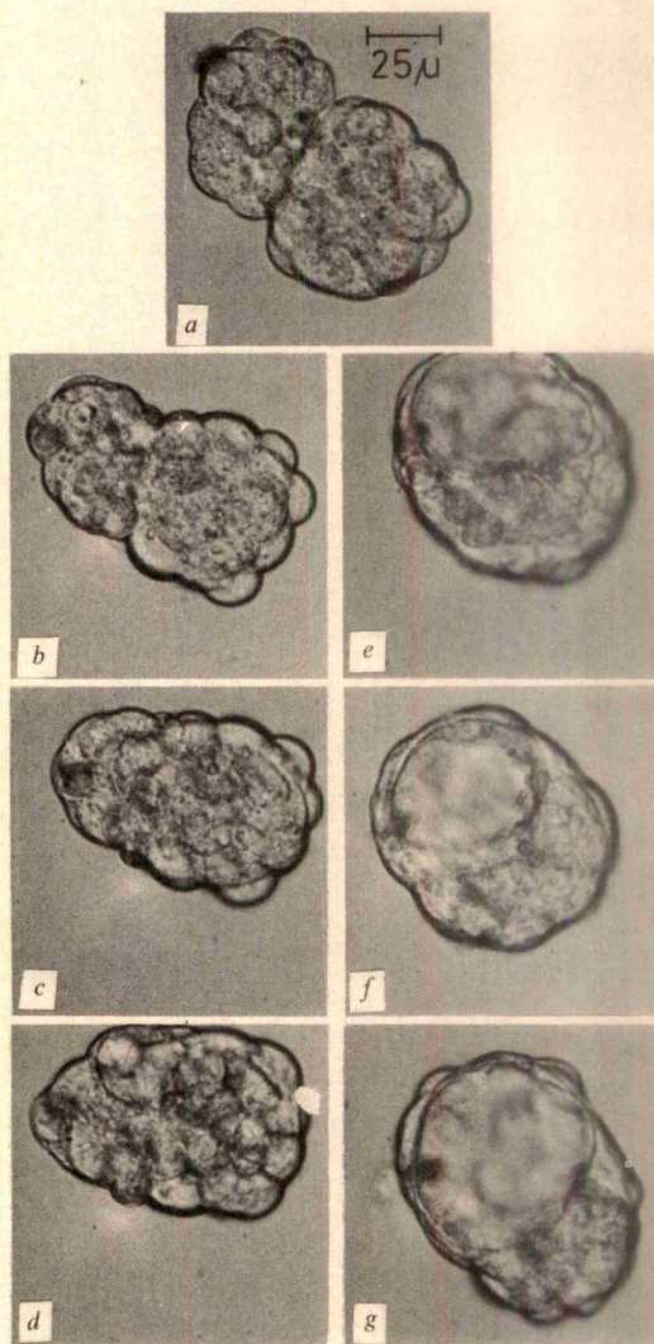
Fig. 1 *a*, Mouse (left) and rat morulae in apposition, shortly after withdrawal of egg holders. Developmental stages after 2 (*b*), 4 (*c*), 6 (*d*), 8 (*e*), 11 (*f*) and 12.5 h (*g*). In *d* the blastocoelic cavity is formed.

ness, the middle of the dark period at midnight. Rat morulae (R, Amsterdam Wistar, 8–16 cell stage) were isolated by flushing on day 3 at 2130 h. The isolated morulae were stored separately at 37° C under oil and 5% CO_2 in air in pyruvate containing culture medium[5].
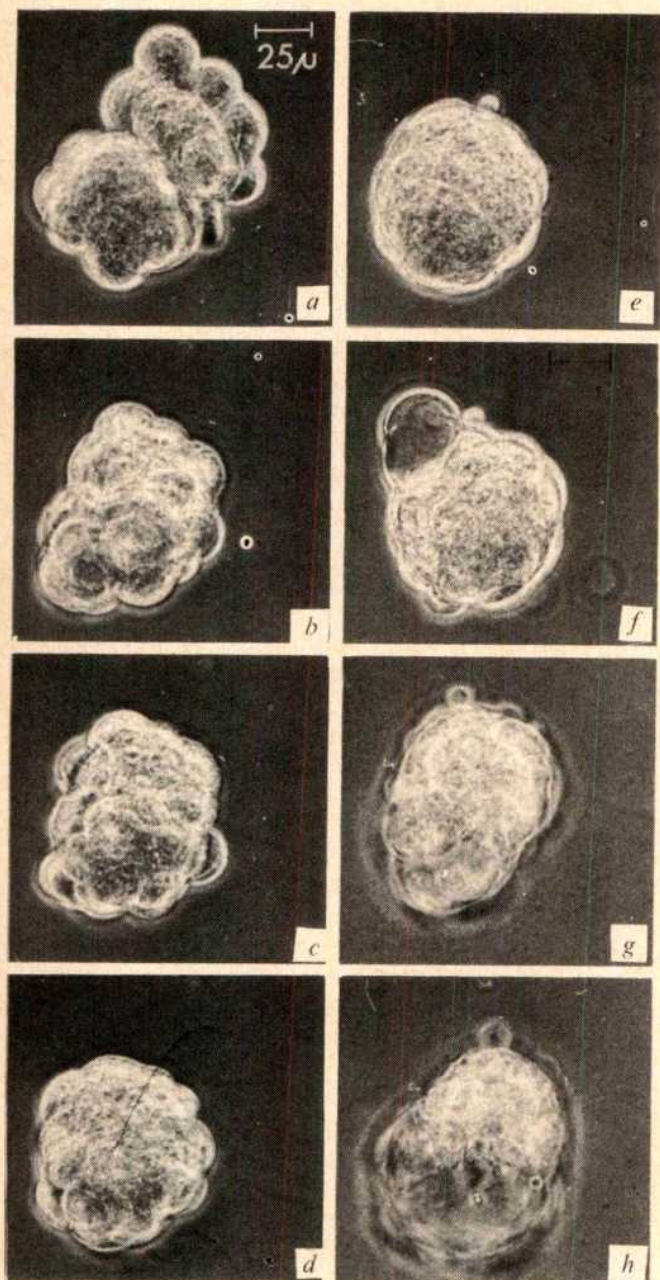
Fig. 2 Mouse (left) and rat (upper right) morulae in the process of fusion. Pictures taken after 30 min (a), 2 (b), 6 (c), 8 (d), 12.5 (e), 18.3 (f), 24 (g) and 34 h (h). Borderline between rat and mouse morulae still visible in (e). First cavity formed in (f), final cavity in (g).

The zona pellucida was dissolved by incubation of the eggs for 3 to 5 min in 0.5% pronase[6]. Final removal of the zona occurred in culture medium by forcing the eggs through a narrow pipette. In each experiment one mouse and one rat morulae were brought into contact in an oil drop culture at 37° C by means of 2 egg holders with a closed lumen[7] driven by a micromanipulator. During this apposition phase, which lasted 20 to 30 min, the Petri dish was not closed but a humid gas stream was directed over the oil surface in order to maintain pH and osmolarity of the medium.

After removal of the egg holders the development of the pair of morulae was followed continuously with a time-lapse movie camera connected to the inverted microscope. Photographs were taken every 30 s with flash light.

A total of sixteen identical experiments were carried out and, in twelve, successful aggregation had occurred in which both aggregate partners showed active proliferation as judged by the temporary bulging of dividing cells at the surface of the large morulae. Sometimes the individual morulae could be recognized for a long time after aggregation by a slight indentation. The way in which the blastocoelic cavity formed varied. In certain cases it appeared where the junction between the two morulae could be seen earlier (Fig. 1b–d), in others an abortive blastocoelic cavity formed in one of the partners (Fig. 2f), which disappeared later. In the same aggregate the lasting cavity formed in the other partner (Fig. 2g). In one experiment one of the aggregate partners formed a cavity before the cell mass had become round (Fig. 3b); this disappeared and a final one was formed after aggregation (Fig. 3d). The pictures and analysis of the time-lapse photographs show that both rat and mouse cells contribute to the formation of a large blastocyst.
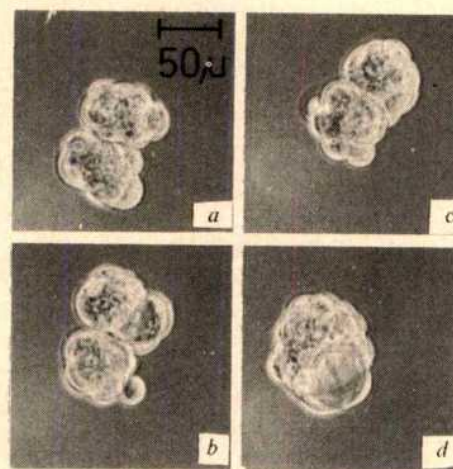
Fig. 3 Fusion of rat and mouse morulae after formation and disappearance of a cavity in the mouse morula. Pictures taken at approximately 30 min (a), 6.6 (b), 10 (c) and 19 h (d).

A general feature of the chimaeric blastocysts was that the inner cell mass was comparatively large.

Preliminary observations have shown that the developmental stage of the rat eggs is critical for successful aggregation and the use of a micromanipulator was also very helpful.

A copy of the time-lapse movie is available for study.

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Effects of Cannabis and Alcohol on Psychological Tests

WE report here psychological data from a combined study on the effect of cannabis and alcohol on simulated car-driving and on psychological tests. The car simulator data showed an effect of cannabis and alcohol on brake time and start time, and a much more pronounced effect of cannabis than of alcohol on time and distance estimation after simulated driving. We have also measured the dose-response curve for cannabis[1]. This report deals with tests of attention and short-term memory, and of subjective and objective ratings of degree and kind of intoxication.

Many of the details are described in ref. 1 and 16. Placebo and double-blind procedures, dose response measurements, and tests for reproducibility and training effects were used, and the subjects acted as their own controls. The effect of a standard dose of alcohol was also studied.

The eight volunteers were healthy men, 21–29 yr old. Three were college graduates and five were skilled workers. None were alcohol or cannabis abusers (that is, no one had a daily alcohol consumption exceeding four drinks; three had never tried cannabis, five had used cannabis from one to fifteen times, nobody more than once a week). The psychological test battery consisted of (A) cognitive tests, (B) consciousness and mood scales, and (C) personality tests. The cognitive tests included: (1) digit span; (2) addition test; (3) subtraction test (serial subtraction of sevens); (4) finger labyrinths (constructed of cardboard plates and thin wooden sticks; the subjects were blindfolded and four different degrees of complexity were used); and (5) Bourdon's cancellation test.

The consciousness and mood scales included (6) Smith and Beecher's mood questionnaire[2] (self-rating scale: the twelve items were rated on a seven-point scale; in our design two more items were added: "motivation" and "kind and degree of intoxication"); (7) an objective questionnaire (rating by experimenter of eleven items covering similar modalities as the Smith and Beecher's questionnaire). The personality tests were for obvious reasons not part of the daily programme and will be described in a later communication, but included (8) the Minnesota Multiphasic Personality Inventory (MMPI) (this test was used during the primary selection of subjects; only subjects without pathological traits according to MMPI profiles were admitted to the study); (9) the Rorschach test; (10) association tests; and (11) interviews.

Both cannabis and alcohol were administered by a double-blind technique and in random order. As a pre-test the subjects were first submitted to the psychological test battery, and driving in the car-simulator. The drug tests were administered 105 min after intake of the cannabis cake (without or with Δ1-THC), and 75 min after a drink of 500 ml. fruit juice (without or with 70 g alcohol), respectively. They consisted of a parallel battery of psychological tests, estimation of kind and degree of intoxication by subject and experimenter, separately, and repetition of simulated car-driving. The next morning (16 h from zero time) the procedure was repeated: (1) a parallel battery of psychological tests; (2) repetition of simulated car-driving; and (3) interview on drug (or placebo) experience. The main research period covered 9 weeks. Each subject completed 9 research days with weekly intervals. The 9-week period was subdivided into three 3-week periods or parts. Part I and part II were designed to compare cannabis and alcohol effects, part II being an exact repetition of part I, except for a new rotation due to continued randomization. Part III was designed to study the dose-response relation for cannabis.

Cannabis resin in original form and baked into cakes was analysed in three different laboratories in Denmark and the USA by gas-chromatography and thin-layer chromatography. Consistent results indicated that the Δ1-THC content was 4%; 200, 300, and 400 mg cannabis resin thus correspond-

ing to 8, 12, and 16 mg Δ1-THC. The inactive cannabis resin used for placebo cakes had a negligible THC content[1].

Non-parametric statistics[3] (Wilcoxon's matched pairs signed ranks test) were used throughout the study. To counterbalance the effects of practice, day-to-day and test-to-test variation, each subject was his own control, both on each research day and in between-days calculations. The results from part I and part II were pooled in the final analysis, because training effects were found to be small compared to drug induced changes.

Table 1 Average Time Spent on Addition by Eight Subjects

Treatment	Pre-test (s)	Drug test (change %)	Post-test (change %)
Placebo	22.7	6	3
Cannabis 300 mg	22.4	37*	8
Alcohol 70 g	22.5	28	1
Cannabis 200 mg	22.1	7	3
Cannabis 300 mg	21.1	37	0
Cannabis 400 mg	20.3	56*	12

Average time spent on addition of four vertical rows of twenty single digits. Change in per cent indicates differences between drug test or post-test and pre-test values. Top half is accumulated data from parts I and II (cannabis versus alcohol), bottom half from part III (dose-response relationship for cannabis).

* P<0.05.

Table 2 Average Time Spent on Subtraction by Eight Subjects

Treatment	Pre-test (s)	Drug test (change %)	Post-test (change %)
Placebo	25.8	0	−2
Cannabis 300 mg	25.6	57*	0
Alcohol 70 g	26.5	46	−2
Cannabis 200 mg	21.3	9	9
Cannabis 300 mg	21.4	21*	3
Cannabis 400 mg	23.3	57*	−10

Average time spent on serial subtraction of sevens starting from a number between 100 and 106. Change (%) indicates differences between drug test or post-test and pre-test values. Top half is accumulated data from parts I and II (cannabis versus alcohol), bottom half from part III (dose-response relationship for cannabis).

* P<0.05.

Table 3 Average Time Spent on the Finger Labyrinth by Eight Subjects

Treatment	Pre-test (s)	Drug test (change %)	Post-test (change %)
Placebo	94.9	4	−1
Cannabis 300 mg	99.4	19*	−12
Alcohol 70 g	91.6	24	−4
Cannabis 200 mg	74.1	19	−2
Cannabis 300 mg	73.0	51*	−3
Cannabis 400 mg	75.6	54*	−11

Average time spent on passing through the most complex out of four finger labyrinths. Change (%) indicates differences between drug test or post-test and pre-test values. Top half is accumulated data from parts I and II (cannabis versus alcohol), bottom half from part III (dose-response relationship for cannabis).

* P<0.05.

There was no significant change in digit span after either cannabis or alcohol. On the addition tests, 200 mg of cannabis resulted in a 7% increase in time taken, 300 mg, a 37% increase, and 400 mg, a 56% increase (Table 1). The differences in errors were not statistically significant either after cannabis or after alcohol. A similar pattern was seen in serial subtraction of sevens (Table 2) with time increases after cannabis of 9%, 21%, and 57%. The error score did not change after alcohol and showed only slight increase after cannabis. In the finger labyrinth test (Table 3) both time and error scores were generally more influenced by the drug, the more complex the labyrinths and instructions. Cannabis at 300 and 400 mg increased time scores in the three more difficult labyrinths, alcohol having a similar but in this case not statistically
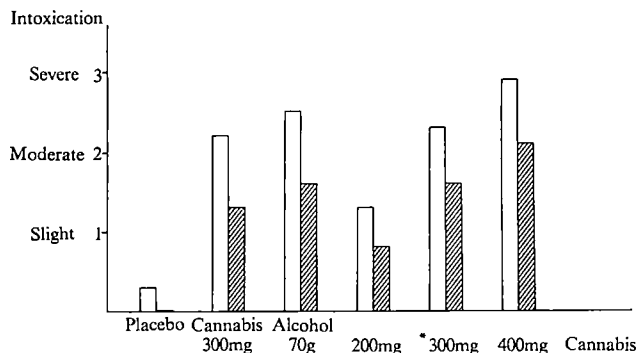
Fig. 1 Rating by subjects (white columns) and by experimenters (hatched columns) of degree of intoxication midway during drug test (~105 min after cannabis and 75 min after alcohol administration). Cannabis contained 4% Δ1-THC. Average from eight subjects. * Values for seven subjects. Left half is accumulated data from part I and part II (cannabis versus alcohol), right half from part III (dose-response relationship for cannabis).

significant effect. The effect of cannabis on errors was more marked than that of 70 g alcohol. There were irregular dose-response trends for cannabis both on time scores and on errors. Sustained attention (Bourdon's cancellation test) was not influenced by cannabis or by alcohol as measured by number of scanned letters. A slight increase in errors was seen after alcohol.

In the Smith and Beecher's subjective questionnaire cannabis and alcohol produced consistent changes on the category "mental clouding", including the three dimensions: alert/mind slow, dreamy/not dreamy, clear-headed/groggy. For alcohol, statistical significance was obtained on the clear-headed/groggy dimension, for cannabis statistical significance was obtained on all three dimensions. The changes were in the direction of "mind slow", "dreamy", and "groggy". On the category "inactivity", including the dimensions sleepy/awake and peppy/no-pep there was a tendency for the subjects to rate themselves more sleepy and less peppy after cannabis. There was a dose-response relationship for the dimension peppy/no-pep.

On the clear-headed/groggy dimension, the experimenters' ratings of the effects of both alcohol and cannabis were statistically significant for all treatments except for the smallest dose of cannabis 200 mg. Sleepiness seemed similarly strongly related to cannabis and, to a lesser extent, lack of motivation and incoherent speech. The dimensions clear-headed/groggy, talkative/silent, and high spirits/low spirits were influenced by alcohol to a statistically significant degree. The changes were in the direction "groggy", "talkative", and "high spirits". Combined results of the subjective and objective rating of intoxication (Fig. 1) showed that in general the subjects rated themselves more intoxicated than did the experimenters. Otherwise the result showed strong agreement between subjects and experimenters: subjectively and objectively six out of eight subjects were rated intoxicated by cannabis after 200 mg, and all eight subjects were rated intoxicated by cannabis after 400 mg; after 70 g alcohol all eight subjects were rated intoxicated by alcohol. Two subjects rated themselves intoxicated by cannabis after placebo and one subject was rated intoxicated by cannabis after placebo by the experimenter.

The results obtained at post-test the following morning are not described in detail because the post-test values never differed to a statistically significant extent from the pre-test values (as seen in the tables).

Most earlier experiments have failed to show a relationship between subjective experience of cannabis intoxication and measurable parameters such as visual[4-7] and time[8,9] perception, speech difficulties[10], psychomotor function[4,5], sustained attention[11], and memory span[6,12,13]. Measurable effects have, however, been found on more complex tasks such as reaction time tests involving choice or discrimination, tasks

involving fine coordination[11] some memory tests[14], and other intellectual tasks demanding the retention and coordination of information[15].

Our results[16] are in general agreement with the earlier findings, and we feel that the differential effect of the drug on time and error scores is important. This may be related to the loss of items from short term memory, while long term memory is relatively unaffected; one of our subjects said, "The events of the preceding seconds are lost, but if I wait for a short while, they pop up again".

The large day-to-day variations in the effect of cannabis showed no consistent trend (Tables 2 and 3), and were probably due to a combination of normal physiological variations and the characteristic waxing and waning of cannabis intoxication. The effects of cannabis can clearly be shown by cognitive tests, though the specific character of the intoxication is more apparent phenomenologically; neither subjects nor experimenters were ever in doubt about which drug had been administered, except in a few instances with the smallest dose of cannabis.

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Long-term Interactions of Marijuana and Behaviour in Chimpanzees

MARIJUANA produces differential effects in human naive and experienced marijuana smokers[1], but owing to ethical constraints involved in repeatedly administering marijuana to drug-naive humans, many human experiments have involved only experienced marijuana users as subjects. These constraints, however, are minimal with non-human subjects, and the great majority of animals used in marijuana research have been drug naive. So far, distinguishing between the long-term effects of marijuana in drug-naive and drug-experienced animal subjects has little precedence in the literature. We report here a number of observations, made over a two-year period during our marijuana research with chimpanzees, which indicate that experiential factors may play a major role in the effects of marijuana on complex behaviour.

Most of our recent marijuana-behaviour studies have been performed with a delayed matching to sample task. The experimental paradigm involves presenting one of six sample stimuli on a translucent key mounted on a stimulus-response panel fixed to the chimpanzee's cage. The chimpanzee must press this sample key ten times when the sample stimulus goes out and a delay period is initiated. After the delay a different stimulus is presented on each of the three choice keys mounted below the sample key, one of which is the same as that previously presented on the sample key. If the chimpanzee chooses this stimulus, a 1 g banana-flavoured pellet is delivered into a foodwell located below the keys and the trial ends. If the chimpanzee chooses either of the two incorrect stimuli, the trial is simply terminated and another begun after a 15 s intertrial interval. The stimuli used are three forms ($\times$, $-$, $\triangle$) and three colours (red, blue and green); within a trial all are from the same stimulus dimension, approximately half are colour trials and the other half are form trials. Generally, each chimpanzee completes 100 trials per day. The five adult chimpanzees used in the experiments reported here had previously been administered several doses of a marijuana compound while performing under simple operant schedules of reinforcement[2,3].

Our previous data indicated that the delayed matching-to-sample performance of chimpanzees was disrupted by single marijuana administrations[4-6]. Our first delayed matching-to-sample observations were made during a four month period while running the chimpanzees on various delay values (for example, 0, 5, 20, and 40 s) of the matching task, and assessing the effects of 1.0 mg kg^{-1} Δ^9-trans-tetrahydrocannabinol (Δ^9-THC), the major active ingredient of marijuana, on performance at each delay[4,5]. Subsequently, the chimpanzees were maintained for an additional year on the delayed matching-to-sample task, primarily at a 20 s delay, during which time they experienced over 80 additional drug doses ranging from 1.0 to 4.0 mg kg^{-1} Δ^9-THC[6]. Although the behaviour in the first phase of our delayed matching-to-sample observations was asymptotically stable during the time period studied, by the end of the subsequent year the nondrug performance had improved considerably.

To determine whether the original relationship between the disruptive effects of Δ^9-THC and the length of the matching-to-sample delay interval had been maintained across extensive exposure to the behavioural task and drug, the initial delayed matching-to-sample experiment was systematically replicated with the same chimpanzees. In this second phase only delays of 5, 20, and 40 s were used. The basic procedure for both phases involved running the chimpanzees at each delay for a number of consecutive days until the behaviour had stabilized, after which 1.0 mg kg^{-1} Δ^9-THC was administered orally in a vehicle of corn syrup, orange extract, and water. On nondrug days they received the drug vehicle alone; both drug and nondrug doses were administered 2.5 h before the matching-to-sample session.

The mean percentage of correct delayed matching-to-sample responses obtained during each experimental phase is plotted in Fig. 1. A comparison of the nondrug control data for the two phases clearly indicates that the accuracy of matching responses had improved during the chimpanzee's year-long exposure to the delayed matching task. In both phases, matching accuracy decreased as the length of the delay interval was increased. This inverse relationship was significant for both phase 1 (F = 46.6; d.f. = 3, 12; P < 0.01) and phase 2 (F 10.5; d.f. = 2, 8; P < 0.01); however, Fig. 1 indicates that the delay values at which Δ^9-THC produced a significant impairment in matching accuracy had changed between phases 1 and 2.
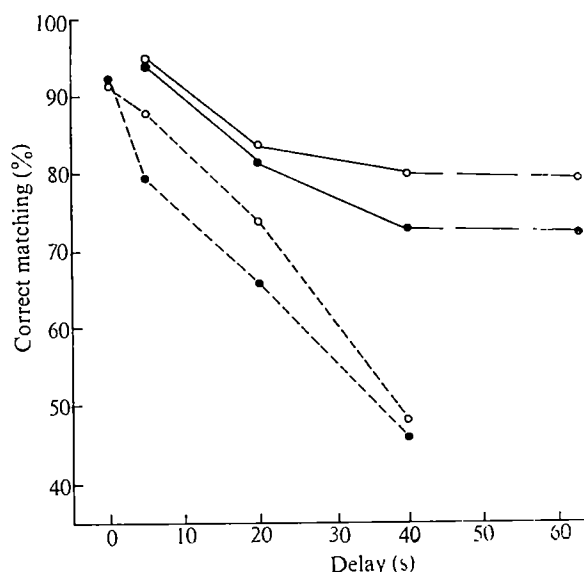
Fig. 1 Mean percentage of correct delayed matching-to-sample responses obtained during nondrug control (O) and 1.0 mg kg^{-1} Δ^9-THC drug (●) sessions at several delay values. Data for phase 1 (- - - -) were obtained approximately one year before the data for phase 2 (———). Data points for the 63 s delay were obtained shortly after phase 2.

Multiple t-tests for the first phase of our observations showed that only the drug effects obtained at the 5 and 20 s delays were significant relative to nondrug control responding (respective ts = 3.9 and 3.4; d.f. = 4; P < 0.05). The absence of a Δ^9-THC effect on the 0 s delay was observed by Zimmerberg et al.[7] and may be interpreted to mean that the drug-produced impairments in matching accuracy were not primarily due to losses of attention or to distortions in perceiving the stimuli presented. Instead, the effects of Δ^9-THC would seem to be specific to that aspect of the delayed matching task which involves short-term memory. Lack of a drug effect at the 40 s delay may have been due to the fact that nondrug matching accuracy at this delay value approached chance performance (33% correct) for some chimpanzees. In contrast, in phase 2 of the experiment, little or no drug effect was observed at 5 and 20 s delays and only the drug effect obtained at the 40 s delay was statistically significant (t = 2.8; d.f. = 4; P < 0.05).

Drug effects obtained during phase 1 at 5 and 20 s delays were not replicated during phase 2 which suggests that tolerance developed to the effects of Δ^9-THC on matching performance at these delays. Whether this tolerance was due to the additional behavioural training received by the chimpanzees during the intervening year or to the fact that they had become more experienced with Δ^9-THC, or both, cannot easily be determined from this experiment. One interpretation is that higher levels of matching accuracy are not as readily impaired by Δ^9-THC as are lower performance levels, and data obtained at the 0 s delay in phase 1 and at the 5 and 20 s delays in phase 2 are consistent with this. That is, matching behaviour at these

delays may have been so well learned that it was not susceptible to the disruptive effects of the drug; however, as can be seen in Fig. 1, nondrug matching accuracy at the 5 s delay in phase 1 was somewhat higher than it was for the 20 s delay in phase 2 and a significant drug effect was obtained for only the former condition. On the other hand, in a test run between phases 1 and 2 of the present experiment[6], there was no indication of tolerance development to Δ^9-THC when chimpanzees were dosed for 21 or 42 consecutive daily sessions under the same 20 s delayed matching-to-sample task.

Observations suggested that the intermixing of drug and nondrug experiences, as well as the number of drug experiences, may be important to the development of Δ^9-THC tolerance. Subsequent to phase 2, animals were maintained at a 40 s delay value and were again administered 1.0 mg kg^{-1} Δ^9-THC on two occasions separated by several nondrug days. The last of these drug administrations produced a minimal decrease in the percentage of correct matching responses from 80.1% (nondrug control) to 77.5% (drug). This latter drug-produced decrease in matching accuracy did not reach statistical significance ($t=0.97$; $d.f.=4$; $P>0.10$), thus again demonstrating tolerance to Δ^9-THC, in this instance at the long matching-to-sample delay of 40 s. As this latter tolerance had developed quite rapidly, we attempted to determine whether the drug was still behaviourally inactive by increasing the length of the delay interval still further to 63 s. The chimpanzee's nondrug performance at this delay quickly stabilized at approximately 80% correct matching, under a 1.0 mg kg^{-1} dose of Δ^9-THC, matching accuracy was significantly decreased to 72.7% ($t=2.8$; $d.f.=4$; $P<0.05$). The nondrug control and drug data for the 63 s delay have been included in Fig. 1 as part of phase 2.

A definite pattern of long-term marijuana-behaviour interactions had been established; reliable Δ^9-THC effect was first produced at a short matching-to-sample delay value; continued intermixing of nondrug and drug sessions at that delay value was accompanied by a reduction in the drug effect. By increasing the length of the delay, a statistically reliable drug effect was again obtained but diminished after the chimpanzees had experienced a number of nondrug to drug transitions at that delay, and so on. It is difficult to offer a pharmacological explanation for our observations that tolerance developed to Δ^9-THC effects at a particular delay value but did not persist when the length of the delay was increased. Indeed, it seems more appropriate to suggest that the observed tolerance was the result of the chimpanzee's learning to perform behaviour which compensated for the drug effects produced in a particular delay situation. Repeated exposures to a defined delayed matching-to-sample task under mixed nondrug and drug conditions may provide the chimpanzee with sufficient opportunities to acquire responses which counteract the detrimental behavioural effects produced by Δ^9-THC in that specific delay situation[8].

Although the nature of these learned compensatory responses cannot now be specified, a comparable adjustment process may occur in human marijuana smokers. In general, the performance of experienced human marijuana users on behavioural tasks is not as susceptible to the disruptive effects of marijuana as is that of drug-naive humans even though the subjective effects of marijuana may become more intense with repeated drug experiences[1]. Nevertheless, there are several implications of the present hypothesis which are in need of direct empirical verification. Most importantly, it would seem that once compensatory responses had been learned in a specific stimulus situation, tolerance to drug produced behavioural effects in that situation should be relatively permanent. That is, at least a partial tolerance should be retained even after a long-term abstinence from both the drug and the stimulus situation had been enforced, but no data for Δ^9-THC are available, even of an indirect nature, which support this implication.

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T-mycoplasmas as a Possible Cause for Reproductive Failure

T-MYCOPLASMAS have been found associated with low birth weight[1] and have been isolated from the foetal membranes in cases with repeated spontaneous abortions[2-4]. It has been suggested, therefore, that T-mycoplasmas might be important for human reproductive failure. Recently, these findings have been supported by Caspi *et al.*[5] who reported a case with amnionitis due to T-mycoplasmas.

We have investigated the possible role of mycoplasmas in human reproductive failure in patients with primary sterility. Before the patients were included in the study they were subjected to a careful clinical examination. All females had normal pelvic examinations, biphasic basal body temperature curves, no signs of a deficient luteal phase (as examined by plasma progesterone values and an endometrial biopsy). All had regular pelvic roentgenological findings. All males had more than 20 million sperm cells per ml., less than 40% morphologically abnormal forms and a good sperm motility in four ejaculates examined within a period of 12 weeks. A total of fifty-two married couples with a primary sterility of 5 yr duration or more were included in the study. Two ejaculates and three specimens of cervical mucus were obtained from each couple and cultured for mycoplasmas with standardized techniques[6,7]. The results obtained were compared with the results of two control groups with proven fertility; cervical cultures from pregnant females attending the ante-partum care clinic (group II) and ejaculates from males, married to pregnant or recently delivered women (group III).

T-mycoplasmas were isolated from ninety-two of the 104 patients in group I (89%) (Table 1). T-mycoplasmas were

Table 1 Growth of T-mycoplasmas in Cervical Mucus and Seminal Fluid in Infertile (I) and Fertile (II, III) Patients

Group number	I		II	III
Sex	♂	♀	♀	♂
Growth of T-mycoplasmas	45	47	9	6
No growth	7	5	31	17
Total number of patients	52	52	40	23

isolated from the cervix of nine of the forty pregnant women in group II (23%) and from the ejaculates of six of the twenty-three men in group III (26%). "Conventional" mycoplasmas, mostly *M. hominis*, were isolated only occasionally from cervical mucus or ejaculates. The difference in incidence of T-mycoplasmas between infertile (group I) and fertile patients (groups II and III) was found highly statistically significant ($P < 0.001$).

After an observation period of 3 months both husbands and wives in group I were treated with doxycycline in recommended dosage for 10 days between the seventh and the sixteenth day of the menstrual cycle in order to eradicate the T-mycoplasmas and to evaluate if this had any influence on the patients with regard to their fertility status or not. If no pregnancy ensued the treatment was repeated during the next two months at the same period of the menstrual cycle. During the fourth and fifth month the patients were treated with doxycycline in increased dosage: 200 mg daily from the seventh to the sixteenth day. If pregnancy was reported, no further treatment was given.

In the ten males and eleven females studied in detail the concentrations of doxycycline in serum varied between 0.4 and 1.35 µg ml.$^{-1}$ 12–14 h after the last dose of doxycycline, while those in ejaculates varied between 0.2 and 1.8 µg ml.$^{-1}$ (mean value 0.95 µg ml.$^{-1}$). Most of the isolated T-mycoplasmas were inhibited by doxycycline in concentrations below 0.1 µg ml.$^{-1}$ although some of the isolates had MIC:s up to 0.6 µg ml.$^{-1}$. The T-mycoplasmas disappeared from all ten males and from all but two of the eleven women studied in detail.

The patients were observed carefully for 5 months. After 3 months pregnancies had been reported in twelve couples. After 5 months another three pregnancies were reported.

It is suggestive that 29% of the women in group I became pregnant within a few months after the eradication of their T-mycoplasmas, after their earlier longstanding infertility. The results of this investigation therefore support the suggestion that at least some T-mycoplasmas may be of importance in some cases with reproductive failure where no other cause is detected.

These findings are now being further investigated.

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Human Lymphocyte Antigen Association in Ankylosing Spondylitis

A STUDY of human lymphocyte phenotypes in unrelated Caucasian individuals with ankylosing spondylitis has revealed a striking similarity in their antigenic pattern. The lympho-cytes of fifty such patients, when tested against a panel of twenty-six different specific typing sera, using a two stage lymphocytotoxicity micro-method, were shown to have in common either the antigen HL-A27 (96%) or the antigen W5 (4%). This remarkably high frequency of the antigen HL-A27 compares with the incidence of 5–6% of this antigen in random Caucasian populations.

Antigen HL-A27 has been shown to have a higher frequency among certain "isolated" communities such as the Pima Indians (10%), (ref. 1). Among these Indians, there is a higher incidence of ankylosing spondylitis than in a random Caucasian population[2], being 5.9% compared with 0.5% or less in the latter group. Likewise, there is a low frequency of this antigen among Negroid populations (0–1%) among whom there is a very low incidence of this disease[3]. These findings support the observation above, details of which will be reported later.

Significant associations between the human lymphocyte phenotype and groups of patients with various diseases involving the lymphatic system have been reported by some authors. The antigens HL-A5, W5 and W18 are found more frequently in patients with Hodgkin's disease[4-6]. Systemic lupus erythematosus is associated with HL-A8 and W15[7,8], adult coeliac disease with HL-A1 and HL-A8[9] and HL-A13 and possibly W17 with psoriasis[10]. HL-A9 and HL-A12 are more frequent in patients with chronic glomerulo-nephritis[11]. The results of two separate studies of patients with rheumatoid arthritis were, however, conflicting and inconclusive[12,13]. An increased frequency of HL-A27 (17%) has been noted in patients with lymphoblastic leukaemia[14]. This is perhaps of relevance to ankylosing spondylitic patients as some of them did develop leukaemia after radiotherapy.

It appears therefore that various HL-A phenotypes are associated with certain diseases. We also postulate that ankylosing spondylitis may be mediated partly by histocompatibility influenced immune responses.

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High Affinity Transport of 2-Deoxyglucose in Isolated Synaptic Nerve Endings

RESULTS of studies of transport in the nervous system using whole brain and slice preparations suffer from the disadvantage that it is not certain whether they apply to capillary, glial, and/or neuronal cells. Isolation of intact synaptic nerve endings (synaptosomes) has made it possible to investigate transport across synaptic membranes which are free of significant glial contamination[1]. Synaptosomes can respire and generate ATP and phosphocreatine with glucose as substrate, and glucose metabolism is largely abolished when synaptosomes are ruptured[2]. The data reported here suggest that carrier mediated sugar transport across synaptic membranes has different characteristics from that seen in brain and brain slices.

Synaptosomes were prepared from rat brain[1,3]. They were inspected by electron microscopy by Dr J. R. Baringer of this department and resembled synaptosomal fractions in published reports. The standard conditions of incubation and assay in all experiments were as follows. Aliquots of the synaptosomal suspension (0.1 ml.) were incubated in triplicate for 15 min at 37° C in 0.5 ml. of a solution (pH 7.4) containing 264 mM sucrose, 26 mM potassium phosphate buffer, and carrying concentrations of ^{3}H-2-deoxyglucose (^{3}H-2-DG) or sucrose. Uptake of radioactive 2-DG into synaptosomes was stopped by adding 5 ml. of 0.32 M ice-cold sucrose and the contents immediately filtered and washed with sucrose on 0.45 μm 'Millipore' filters; the filters were transferred directly to counting vials containing a triton-toluene scintillation solution for determination of radioactivity retained in the synaptosomes[3]. The assay was linear in time for at least 20 min and with increasing protein concentration up to at least 0.8 mg protein. In blank tubes designed to measure non-specific entry of radioactive sugar, 200 mM non-radioactive glucose replaced an equal concentration of sucrose prior to addition of synaptosomes. The large excess of non-radioactive glucose is assumed to prevent specific uptake of ^{3}H-2-DG but not effect diffusion[3]. Radioactivity in synaptosomes in blank tubes was reduced to less than 5% of the total. 2-DG is metabolized only to 2-deoxyglucose-6-phosphate (2-DG-PO$_4$)[4]. Separation of 2-DG from 2-DG-PO$_4$ was carried out by a two step chromatographic procedure using a 2.5×0.5 cm column containing 'Dowex 1–X8', 100–200 mesh. 2-DG is not retained by the column and is eluted with water; 2-DG-PO$_4$ is eluted with 1.4 N HCl.

Rat brain synaptosomes incubated with ^{3}H-2-DG were assayed for uptake by 'Millipore' filtration. Nonspecific entry of radioactivity into synaptosomes increased linearly with substrate concentration and this minor component was subtracted from values obtained with the active system. Specific uptake of radioactivity exhibited saturation kinetics with increasing 2-DG concentration. K_m, the apparent concentration for half-maximal uptake of 2-DG into synaptosomes, was 0.24 mM (Fig. 1). This is 42 to 375 times less than values obtained in brain slices (10–90 mM)[5–9] and indicates that nerve endings have a highly specific transport system for glucose. 2-DG uptake per mg protein by microsomes, mitochondria and synaptosomes ruptured by osmotic lysis or sonication was 4–9% of intact synaptosomes. Insulin (0.02 U ml.$^{-1}$) was without effect on 2-DG uptake whether synaptosomes were prepared from normal rats or animals made diabetic with streptozotocin[10]. After incubation with 1 mM 2-DG under standard conditions ($n=8$), 23% of the radioactivity taken up by synaptosomes was recovered as free 2-DG and 77% ±3.4 s.d. as 2-DG-PO$_4$. Since glucose-6-phosphatase activity is not prominent in the nervous system[11] the presence of free 2-DG inside synaptosomes suggests that 2-DG entered without phosphorylation. Subsequent

phosphorylation of 2-DG, however, might be rate limiting and the K_m for 2-DG uptake in synaptosomes might be a result of hexokinase activity. To determine whether transport or phosphorylation was rate limiting we measured the percentage of free 2-DG and 2-DG-PO$_4$ recovered in synaptosomes after incubation with 1 μM to 5 mM 2-DG ($n=$ 26). If phosphorylation was rate limiting, the percentage of free 2-DG should increase with increasing concentrations of substrate above the K_m for uptake. Instead, we found that the percentage of radioactivity recovered as free 2-DG remained the same despite a 5,000-fold range of substrate concentration. The average was 75.3% ±4.7 s.d. This indicates that phosphorylation of 2-DG is linear with total uptake of 2-DG whereas total uptake of 2-DG is saturable. The K_m for 2-DG uptake in these experiments therefore seems to be determined by transport of 2-DG across the synaptosomal membrane and not its subsequent phosphorylation. Studies carried out with 3-O-methylglucose (3-MG) further support this interpretation.
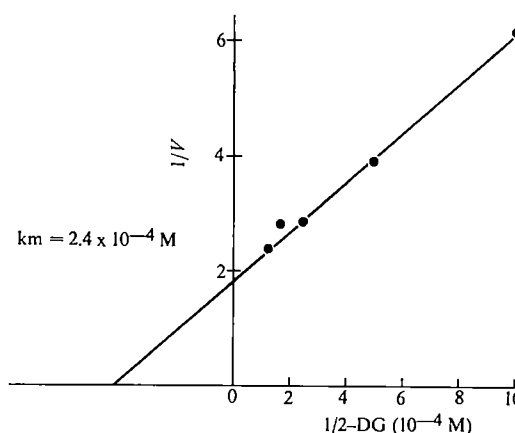
Fig. 1 A Lineweaver and Burke plot of ^{3}H-2-deoxyglucose uptake into synaptosomes containing 0.4 mg protein. The ^{3}H-2-DG specific activity is $7.6×10^5$ c.p.m. μmol^{-1}. $V=$c.p.m.$×10^{-4}$. After incubation with 10^{-4} M 2-DG, the intrasynaptosomal concentration was at least five times greater than the medium. Blank values ranged from 0.03% to 3.8% of the active system with increasing substrate concentration. Each point is the average of three determinations.

3-MG is a non-metabolizable sugar which is transported into brain[12] but does not react with hexokinase and is not phosphorylated[4]. Nevertheless, 3-MG and 2-DG should compete for entry into synaptosomes if they share a common carrier-mediated process. Incubation of synaptosomes with 3-MG depressed uptake of ^{3}H-2-DG; 3-MG is a competitive inhibitor of ^{3}H-2-DG uptake with a K_i of 6.5 mM (Fig. 2a). Even though 3-MG does not react with hexokinase, 3-MG and 2-DG seem to have highly specific affinities for a common glucose carrier in isolated nerve endings.

Phloretin inhibits glucose transport in many tissues but has not been reported to inhibit transport in brain. In synaptosomes, however, phloretin is a competitive inhibitor of 2-DG uptake with a K_i of 0·75 μM (Fig. 2b). This value is probably far below that for inhibition of glucose metabolism[13] and suggests that the drug reacts directly with the glucose carrier in nerve endings. By contrast, phlorizin did not inhibit 2-DG uptake at these concentrations; also NaCl (0.075 M), which replaced sucrose (0.15 M), and ouabain (0.1 mM) were without effect. These findings are consistent with the concept that phloretin tends to inhibit Na$^+$ independent sugar transport[14].

The demonstration of a high affinity glucose transport system is reminiscent of several high affinity uptake processes for amines and amino-acids in synaptosomes which have been described recently[15]. The presence of such high
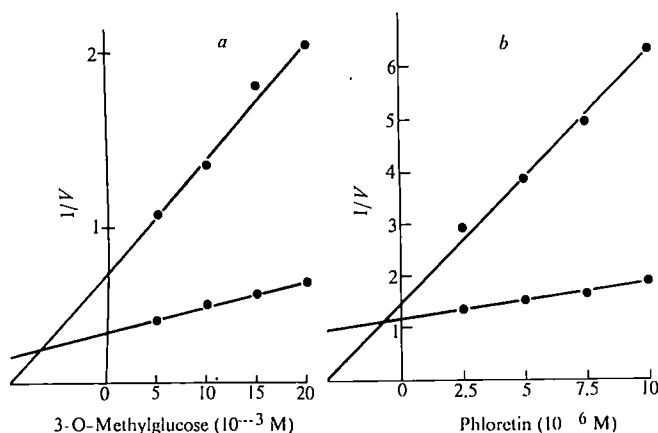
Fig. 2 Dixon plots of 3-O-methylglucose (*a*) and phloretin (*b*) inhibition of ^{3}H-2-DG uptake into synaptosomes containing 0.5 and 0.6 mg protein. The concentrations of ^{3}H-2-DG are 0.1 and 0.4 mM. The ^{3}H-2-DG specific activity is 10^7 c.p.m. μmol^{-1} and 1.8×10^6 c.p.m. μmol^{-1}. The K_i for 3-O-methylglucose and phloretin is 6.5×10^{-3} M and 7.5×10^{-7} M respectively. The conditions are as in Fig. 1.

affinity transport systems for metabolites in synaptosomes provides neurochemical evidence for specific utilization of these metabolites at the synapse. The affinity of 2-DG for transport in synaptosomes is much greater than in brain slices, and phloretin is a potent competitive inhibitor of this carrier-mediated glucose transport system. It is possible that nerve endings have a high affinity glucose transport system to support a high rate of presynaptic energy production. This would be consistent with the observation that dendritic layers in the cortex which contain both nerve terminals and dendrites seem to account for a high proportion of oxidative metabolism in grey matter[16]. On the other hand, synaptosomes (pinched-off nerve terminals) are enclosed by membranes derived from neurones and may reflect membrane properties of axons, neurones and dendrites. Consistent with the observation that neurones exhibit greater oxidative metabolism than glia[17], it is also possible that a highly specific glucose transport system exists only in neuronal membranes. If true, the glucose transport system might be useful in helping to distinguish separated neurones from glial cells.

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Phytogeography of the Fungal Genus *Lycoperdon* in Relation to the Opening of the Atlantic

IN the preparation of a world monograph of the genus *Lycoperdon* (Gasteromycetes) I have examined 8,500 herbarium collections of these puffballs from Europe (only the Baltic region in the case of the USSR) and North America. Abundance of material enabled grid maps to be drawn showing species distribution; such maps are rare in mycology owing to a lack of precise chorological information[1–3]. Fungi were therefore seldom considered biogeographically[4–7] until Kreisel's monograph of *Bovista*[8] in 1967.

Map comparisons showed that *Lycoperdon* species presented well marked distribution types that could be classified into chorological elements comparable with those used for vascular plants (Fig. 1). Among these elements three groups could be distinguished; a subcosmopolitan element (two species); elements with a northern affinity (thirteen species); and those with a southern affinity (fifteen species). Most species from the second group (northern affinity) occur on both sides of the Atlantic while those with southern affinities are, with a single exception, unilateral and are phylogenetically more primitive on purely morphological grounds[9,10]. Endemism is more developed and there are also three European/Eastern American vicarious pairs: *L. atropurpureum* Vitt. and *L. mauryanum* Pat. ex Demoulin; *L. decipiens* Dur. et Mont and *L. rimulatum* Peck; and *L. echinatum* Pers. per Pers. and *L. americanum* Demoulin[11].

Three theories could explain the development in space and time of the genus. Recent long distance dispersal of spores over the Atlantic could explain the occurrence of similar species on both sides; vicarious pairs would be explained by an earlier crossing.

This does not, however, explain the restriction of some species to one continent, nor why those endemics and vicarious pairs only have southern affinities.

Long distance dispersal has been shown by many plant geographers to be overemphasized[12–14]. Crum[15] showed that for Bryophytes it is limited to a few weed species; and I suggest that even for fungi and species such as *Lycoperdon* with wind dispersed spores of low terminal velocity and greater dispersal, oceans are still major geographical barriers. One of the reasons for this might be the loss of germinative ability observed on spores collected over the Atlantic[16]. It is usually considered that pathogenic fungi cannot cross oceans[17–19] except possibly in the trade wind region[20].

If long distance dispersal is not the chief explanation of disjunct distributions, then alternatively somewhere in geological time there was an almost continuous terrestrial biota which favoured stepwise progression of species. Terrestrial migration through the Bering Straits, as for man and other late Cainozoic mammals, has been claimed, but various marine obstacles have existed in Siberia during a greater part of Mesozoic and Cainozoic[21] and also the Bering area never seems to have been hospitable to warm temperate communi-
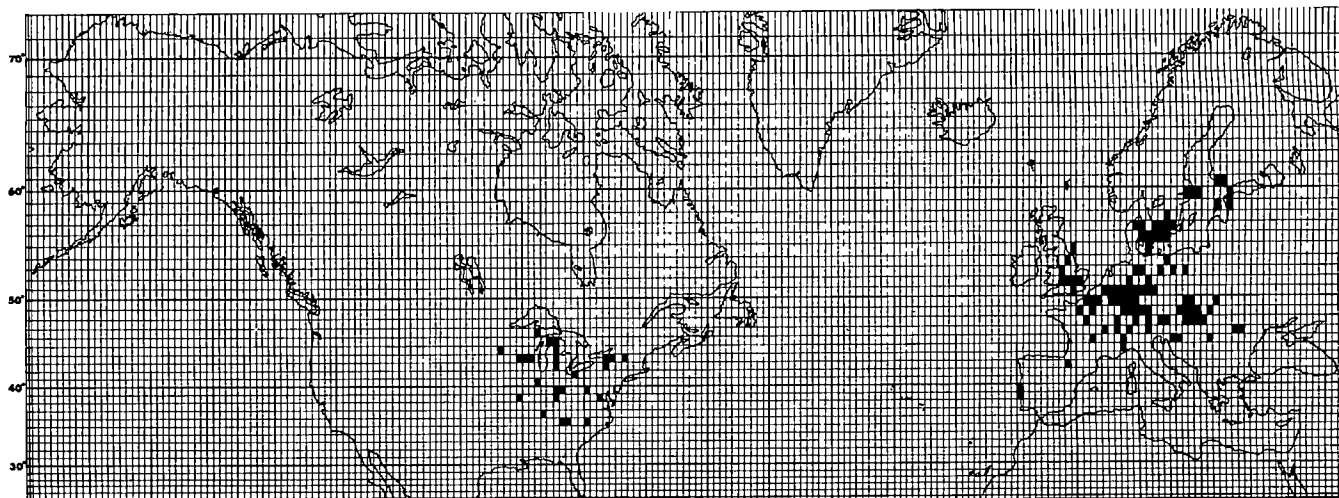
Fig. 1 Areas of two vicarious species, *Lycoperdon americanum* in America and *L. echinatum* in Europe.

ties[22-24]. Florin's maps of the past and present distribution of conifers[25] also argues against exchange of forest elements between Europe and America through Beringia.

Knowledge of plate tectonics[26-29] enables the facts to be much better explained by continental drift than by any long distance or land-bridge theory, and it is now favoured by many biogeographers (refs. 30-41, and reviewed, ref. 42). In light of the drift theory, due to the more easterly position of the American plate, a Beringian land-bridge seems improbable before the Cainozoic[43], and many of the floral exchanges between Europe and North America seem to have occurred through Eastern America and Western Europe before the completion of the Atlantic barrier. This conclusion has already been reached by Axelrod[35] for the Mediterranean–South West USA floras.

Using plate tectonics data[43-46] together with data on the history of climates[23] and floras[22,47], I conclude that since the late Cretaceous, first the North Atlantic, then the Labrador Sea must have started to interfere with the migration of subtropical and warm temperate floras. The junction of the

Norwegian Sea and the Arctic Ocean was not complete before the middle Eocene, allowing free interchange for cool temperate floras especially rich in conifers[48] (Fig. 2). The closing of the Norwegian Sea during the beginning of the Cainozoic is also supported independently of plate tectonics by sedimentology studies[49].

I consider that this explains why northern elements in *Lycoperdon* have not yet shown visible speciation between Europe and America, for not only did the populations remain in direct contact until the middle Eocene, but they were probably still able to exchange genes as long as Arctic regions remained habitable for them and seas were not too wide for easy crossing by wind dispersed spores. Southern elements, which have been separated for a much longer time, show vicariousness and endemism. The primitive morphological characters of the southern species and the richness and diversity of the southern flora suggest development of the genus in warm temperate broad-leafed deciduous forests[50] at a time that preceding considerations and parallelism with the development of modern forest types put as Cretaceous.

This would mean that fungi have evolved rather slowly since the Mesozoic. The fossil record is scanty but it is not in contradiction with this conclusion; the principal groups Phycomycetes s.l, Ascomycetes and Basidiomycetes were already in existence at the end of the Palaeozoic[51-54], polypores in the Jurassic[55], Palaeocene fungal spores with a very modern aspect[56], and Eocene spores attributed to the extant Gasteromycetous genus *Scleroderma*[57] have all been described.

Knowledge of Asiatic *Lycoperdon* is at present restricted owing to a lack of available data. The absence of a species related to *L. echinatum-L. americanum* in Eastern Asia should, however, be noted; it cannot be simply a consequence of lack of notice by collectors, as these fungi are two of the most striking of the genus. A study of Siberian material, which I hope to undertake, should give additional information on the theory described here. A palynological study of cores drilled at the level of the oldest magnetic anomalies at various parts of the North Atlantic and the Norwegian Sea should give biogeographers a picture of the environment of the northward opening ocean.

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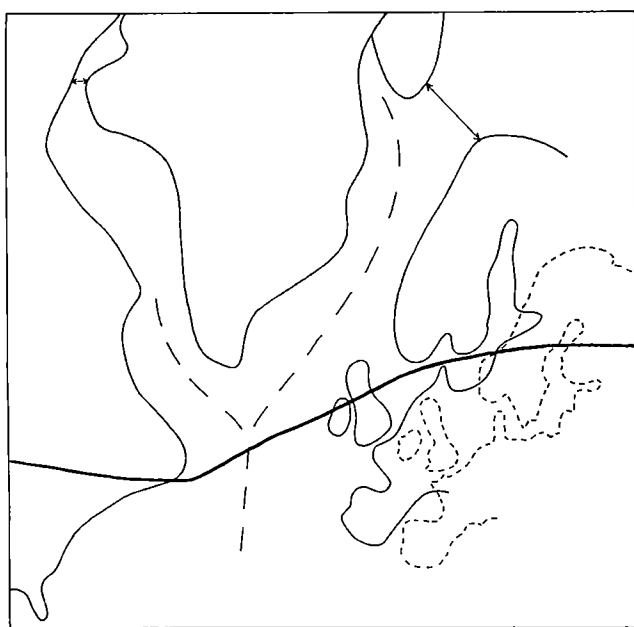
Fig. 2 Schematic position of actual land masses during the Eocene as interpreted from ref. 43. The thick black line is the limit between subtropical and temperate floras according to Takhtajan[22]. - - -, Present position; — — —, oceanic barrier; ←→, possible terrestrial connexion.

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Sativin: an Induced Isoflavan from the Leaves of *Medicago sativa* L.

It has been shown that low-molecular weight antibiotics (phytoalexins[1]) may be produced following the interaction between plants and various biotic or abiotic agents. In tissues penetrated by non-pathogenic fungi the accumulation of phytoalexins may be responsible for cessation of fungal development, which suggests that these compounds may have a role in disease resistance. Phytoalexins can apparently be detoxified by pathogenic fungi[2].

Several phytoalexins have been isolated from species belonging to the Papilionateae subfamily of the Leguminosae[1,2]. In addition to pisatin from *Pisum sativum*[3] and phaseollin from *Phaseolus vulgaris*[4], investigations of species comprising the tribe Trifoleae have resulted in the isolation of demethylhomopterocarpin (structure I) from *Medicago sativa*[5], *Trifolium pratense*[6] and *Melilotus alba* (J. L. Ingham, unpublished observations) and maackiain from *T. pratense*[6] and *Trigonella foenum-graecum* (J. L. Ingham, unpublished observations). These compounds all belong to the pterocarpan sub-class of the isoflavonoids.

I
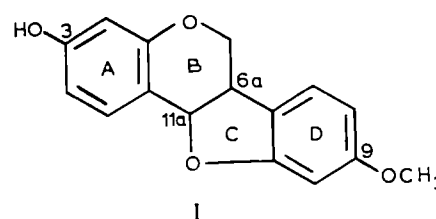
Two antifungal compounds were isolated from infected leaflets of lucerne (*Medicago sativa*). One of these, 3-hydroxy-9-methoxy pterocarpan or demethylhomopterocarpin (structure I) ($\lambda_{max}^{95\% EtOH}$ nm. 209, 227(sh), 282 and 287) had been previously isolated from this plant[5], but the second (for which we propose the name *sativin*) was an isoflavan (structure II) of unknown structure. We report here the detection and characterization of an isoflavan which functions as a phytoalexin.

II
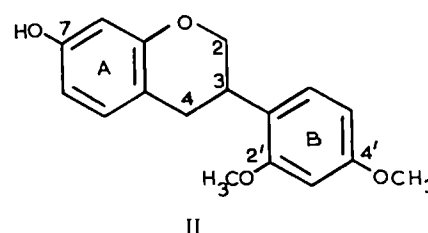
Antifungal materials were obtained from detached leaves by the drop-diffusate technique[7]. Conidial suspensions (about 5×10^4 spores ml.$^{-1}$) of *Helminthosporium turcicum* in 0.05% 'Tween-20' were used as the phytoalexin inducer. Control leaves received drops of de-ionized water containing 'Tween-20'.

After 48 h incubation the droplets (diffusate) were collected and extracted five times with anhydrous ethyl acetate. The ethyl acetate fractions were bulked, reduced to dryness, re-dissolved in 95% ethanol and chromatographed on fluorescent silica-gel thin-layer plates. The developing solvent was a 3:1 (v/v) mixture of chloroform and carbon tetrachloride. In this system sativin had an R_F of 0.44 whilst that of demethylhomopterocarpin was 0.36. Compounds were located on chromatograms either by ultraviolet light or by *p*-nitroaniline reagent[8]. Initially, this reacts with both sativin and demethylhomopterocarpin to produce intense yellow spots, but, whereas the former retains the yellow coloration, the latter rapidly turns a deep orange-brown.

Diffusates were bioassayed directly on thin-layer plates[9]. Irrigated plates were sprayed first with a spore suspension of *Cladosporium cucumerinum* and then with cool, molten 'V-8 juice' agar. After incubation the plates were covered by a grey fungal growth except for those areas corresponding to the location of either sativin or demethylhomopterocarpin. These areas appeared white owing to inhibition of fungal growth. No antifungal activity was detected in control diffusates.

Pure sativin ($C_{17}H_{18}O_4$) is a white crystalline solid possessing a reduced isoflavanoid skeleton substituted with one hydroxyl (OH) and two methoxyl (OCH_3) groups. The mass spectral data (M^+ 286; prominent fragments, m/e 164, 151, 149, 135, 122, 121) indicate an isoflavan ring system. On biogenetic grounds this should be substituted at C-7, C-2′ and C-4′, and should resemble vestitol (structure III), an isoflavan from *Machaerium vestitum* and *Dalbergia variabilis*[10].

III
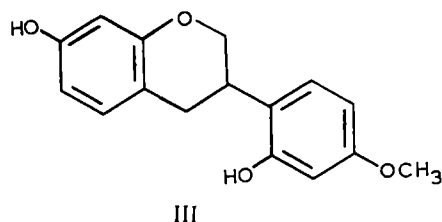
In 95% ethanol sativin has an ultraviolet absorption maxima (nm ($\log_{10}\epsilon$)) at 208 (4.42), 227 (4.01), 280 (3.61), 284 (3.62) and 290sh. (3.42) and minima at 223 (4.00), 251 (2.71) and 283 (3.60). In ethanol containing 0.2 M sodium hydroxide solution, maxima were 216, 248(sh.), 280(sh.), 285 and 296(sh.). Sativin is stable under acid and alkaline conditions and is apparently unaltered by autoclaving at 15 p.s.i. for 30 min. The stability of sativin to refluxing with 4–6% sulphuric acid established that the compound was not a 2′-hydroxyisoflavanone[11]. In acid media such a compound would undergo cyclodehydration with the consequent formation of a 6a,11a-dehydropterocarpan, recognizable by its characteristic absorbance in the visible (330 to 360 nm) region of the spectrum. Acid stability also indicated the absence of hydroxylation at C-3.

Sativin is soluble in many organic solvents including ethyl acetate, ethanol and methanol. It is sparingly soluble in carbon tetrachloride and virtually insoluble in hot (60° C) or cold (15° C) water. Sativin has a melting point of 125–127° C and is optically active, $(\alpha)_D^{22}$—15°. Vestitol has a similar optical rotation (+21.5°) but is dextrorotatory.

Although mass spectral analysis enabled the assignment of the various substituents to either ring-A (hydroxyl) or ring-B (both methoxyl groups) it was considered desirable to prepare synthetically a derivative of sativin, which, when compared with a similar derivative of vestitol, would firmly establish the proposed 7,2′,4′-oxygenation pattern. This aim was achieved by methylation of sativin to IV (7,2′,4′-tri-

IV
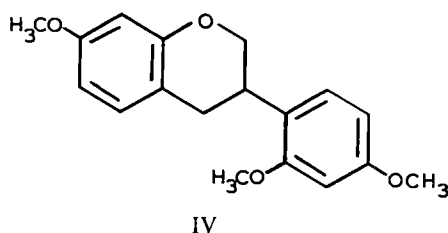
methoxyisoflavan), a compound which can also be prepared by the methylation of vestitol (7,2′-dihydroxy-4′-methoxy-isoflavan). The methylated products of sativin and vestitol possessed identical ultraviolet spectra and mass spectral fragmentation patterns (M^+ 300; prominent fragments, m/e 164, 151, 149, 137, 121) and were chromatographically inseparable in several solvent systems. This demonstrated the 7,2′,4′-oxygenation pattern of sativin and, together with the mass spectral data, firmly established the substitution pattern of the aromatic rings.

The absolute configuration of sativin is R, which follows from its co-occurrence with, and possible derivation from, 6aR,11aR-(—)-demethylhomopterocarpin. This compound presumably undergoes enzymic cleavage of the dihydrofuran ring (C) followed by selective methylation to sativin. (—)-Vestitol may be an intermediate in this transformation.

When incorporated into agar and tested against the mycelial growth of *H. turcicum*, sativin possessed a median effective dose (ED_{50} value of 15 μg ml.$^{-1}$). In contrast, demethyl-homopterocarpin had an ED_{50} value of 25 μg ml.$^{-1}$. In diffusates the ratio of sativin to demethylhomopterocarpin was approximately 2:1 whilst quantitative analysis of the leaf tissues underlying the droplets consistently revealed a sativan/demethylhomopterocarpin ratio of 5:1. We suggest that sativin has an important role in the disease resistance of lucerne leaflets.

The ring structure of sativin occurs in at least seven other natural products. All known isoflavans except for the animal metabolite, equol[10], have been isolated from the Papilionateae subfamily of the Leguminosae. They include vestitol and mucronulatol from species of *Machaerium* and *Dalbergia*[10], lonchocarpin and laxifloran from *Lonchocarpus laxiflorus* and licoricidin from *Glycyrrhiza glabra*. This is the first description of the isolation of an isoflavan from a species belonging to the tribe Trifoleae. We suggest that because of the marked antifungal activity of sativin and other phytoalexins from the Leguminosae, these, or structurally related synthetic products, may be useful in crop protection.

Full details of this work are in preparation. We thank Professors W. D. Ollis and O. R. Gottlieb for samples of (+)-vestitol.

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Spittlebug Polymorphic for Warning Coloration

LINDROTH[1] suggests that some insects gain a selective advantage by mimicking other insects whose striking colour patterns serve to warn potential predators of an unusually effective escape mechanism. The mimicked insects hop suddenly when disturbed, greatly lessening the probability of a predator's success. A learning predator comes to associate particular colour patterns with wasted effort and spurns both the model and the relatively sluggish mimic, so long as encounters with the model substantially outnumber those with the mimic. Lindroth's

hypothesis may help explain cases of apparently aposematic (warning) coloration in non-mimetic animals which are neither poisonous, distasteful, nor formidably outfitted for defence, but which possess efficient close quarter escape mechanisms[2]. I propose that the phenomenon of escape warning coloration may be an important factor in the colour polymorphism of *Philaenus spumarius* (L.), the common meadow spittlebug.

This species is one of the most common insects in many North American and Eurasian temperate habitats. It exhibits extensive colour polymorphism, with the number of colour forms and their relative frequencies varying from area to area. Here I limit analysis to the relatively simple polymorphic situation prevailing in the southern Great Lakes region of the United States where only four colour forms (Fig. 1) occur at frequencies exceeding 1%[3,4]. Breeding experiments in Finland indicate that the colour forms are determined by a series of allelic genes (or supergenes) ordered in a dominance hierarchy[3]. *Populi* and *typica* phenotypes are distinct in males but intergrade in females and represent alternative expressions of one allele. The *trilineata* allele is expressed in both males and females, the *marginella* allele only in females. In heterozygous condition *marginella* is dominant to *populi-typica* (in females) and *trilineata* is always dominant to both these alleles (Halkka, personal communication).
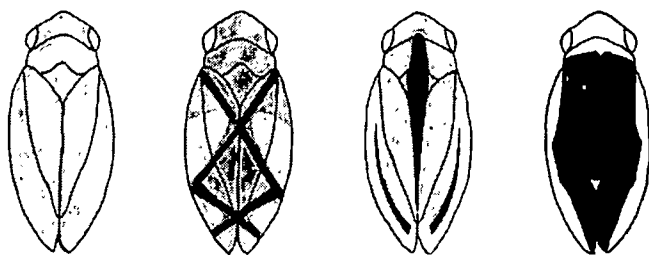
Fig. 1 Main colour forms of *Philaenus spumarius* in southern Great Lakes region. Left to right: *populi, typica, trilineata, marginella*. Actual insect length about 6 mm.

Recent authors[4-6] attribute the variety and maintenance of the *P. spumarius* colour polymorphism to apostatic[7] selection. According to this hypothesis rarer colour forms, even if they are relatively conspicuous, are neglected by predators hunting for prey on the basis of a "search image" formed during their initial contacts with the more common colour forms. Rare forms increase in frequency and common forms decrease until at the frequencies observed in nature all forms have equal probabilities of survival and reproduction. This hypothesis does not explain why particular colour forms have evolved as they have or why their geographical distributions vary in the way that they do. Lindroth's idea provides an approach towards solving these last two puzzles for at least one colour form, *marginella*.

Populi, typica, and *trilineata* individuals range in colour from light straw or grey through various shades of nondescript brown with patches or lines of darker brown or black. They appear to be cryptically coloured against a number of natural backgrounds. In contrast, *marginella* individuals with their dark black bodies outlined by cream white on three sides often stand out strikingly from their surroundings. Bold patterns of black and white recur in nature as a theme of warning coloration[8], and the distinctiveness of the *marginella* colour pattern in *P. spumarius* strongly suggests such a role. The species is not foul tasting (personal observation) or outfitted with obvious aggressive defence mechanisms, and so might seem to lack the ordinary prerequisites for warning coloration. But its back legs, like those of other spittlebugs, are specially modified for hopping. It can fly, but when disturbed it usually jumps abruptly, landing awkwardly several feet away[9], safely removed from the vicinity of a potential predator.

A learning predator will recall more vividly a frustrating encounter with *marginella* than a similar encounter with one of the more anonymous colour forms. To the degree that such encounters lead predators to shun *marginella* more than other colour forms, selection will favour *marginella*. If as *marginella* becomes more frequent in a population the selective disadvantage of being common begins to outweigh the advantage of being conspicuous, a balanced polymorphism will result.

The geographical distribution of colour forms and the biology and ecology of *P. spumarius* lend some support to this interpretation. Around the southern Great Lakes the frequencies of most colour forms vary from area to area. *Trilineata*, for example, ranges in frequency from 1% in east central Illinois to 10% in west central Wisconsin. In contrast the relative abundance of *marginella* is remarkably even over the region, comprising about 5% of all females[3], in spite of the variety of physical and biological environments the species encounters. But while the species occupies many habitats, its primary habitat throughout the region is fields of leguminous forage crops (principally alfalfa, *Medicago sativa*) where it regularly achieves very high densities (more than 300 adults/m²)[10]. Each summer as the fields are mown large numbers of adults disperse over surrounding habitats, swamping local non-pest *P. spumarius* populations. These marginal but substantial populations of woods, roadsides, fencerows, and abandoned land may owe their very existence to the yearly influx from hayfields, a phenomenon thoroughly documented for one old field in south-eastern Michigan[10]. This species migration pattern strongly suggests that selective forces operating in fields of forage crops determine *P. spumarius* gene frequencies over the entire region in question. Though the particular forage crops grown and mean climatic factors may vary considerably from area to area within the region, the basic structure of predator-prey relations in the ecology of the fields remains the same, and the frequency of *marginella*, probably determined by these relations, is relatively constant.

The dark black body of *marginella*, in addition to its purely visual role, may assist quick warming in the morning Sun for added mobility in a form that depends for its survival on a reputation for fast getaways. The limitation of *marginella* expression to females probably reflects the fact that, although the species mates soon after adult emergence in June, there is a mechanism for delayed fertilization[11] and the females do not begin to oviposit until September[9,10]. The females carry the species' gametes throughout the summer and must bear the brunt of selection for predator avoidance. In the early summer, probably the only time of selective importance for males, learning predators have had little time to accustom themselves to the pursuit or avoidance of particular colour forms, and the presumed advantages of the *marginella* pattern would be slight or absent. Interestingly, *Neophilaenus lineatus*, a relative of *P. spumarius*, begins laying eggs in early July, soon after adult emergence and mating[12]. Although this species is also a widespread pest and reaches high densities in grass meadows in the eastern USA, it is monomorphic.

Conclusive evidence that *P. spumarius* is polymorphic for escape warning coloration will require detailed study of its predator-prey relationships, particularly in alfalfa fields. Birds and spiders are probably major predators[10] and there is good evidence that spittlebugs furnish a significant food source for some sparrow species in south-eastern Michigan (F. C. Evans, unpublished data). Beyond this we know little.

Finally, my arguments apply to a single colour form in a single region. In many other regions the polymorphism is more complex. Even in the region in question it is undoubtedly governed by many more factors than I have included in this analysis.

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Non-Circadian Photoperiodic Timing in the Aphid *Megoura*

The modification of development by the timing of light and darkness, photoperiodism, is well-known among plants, birds, mammals and insects, and its widespread occurrence raises the question of whether it operates by different mechanisms in different instances. The view that all photoperiodism has a common basis is supported by evidence that it often involves an endogenous circadian rhythm (ECR) or "biological clock" that oscillates with similar properties in unrelated organisms[1,2]. There have been experiments which suggest that one of the systems most carefully studied, the control of sexual and asexual reproduction in the aphid *Megoura viciae*, proceeds through a non-rhythmic, non-oscillating timer of a different kind[3,4]. Here I report another experiment which provides good evidence against even a rudimentary form of circadian timing in *Megoura* photoperiodism.

The circadian rhythmicity of photoperiodic timing has been inferred from several kinds of evidence; sensitivity to brief light exposures during long dark periods may show maxima or minima roughly 24 h apart, and light/dark cycles with overall periodicities close to 24 or 48 h may have unique effects. A more complex type of experiment involves so-called "skeleton photoperiods". Instead of a normal daily cycle such as 8 h of light alternating with 16 h of darkness (here abbreviated as 8(16)) a schedule such as 1(6)1(16) can be used, in which the 8 h light period is represented by its "skeleton", a dark period started and terminated by brief light exposures including a total span of 8 h. Circadian rhythms in quite diverse phenomena, such as pupal eclosion in the fly *Drosophila* and carbon dioxide output by cultures of the duckweed *Lemna*, respond similarly to skeleton photoperiods in several ways[2,5,6]. In this context it is important that when the two portions of the skeleton photoperiod are nearly equal, for example in 1/4(10½)1/4(13), the effect on the oscillation of the rhythm depends on which of the two dark periods is presented first (after continuous light).

This result prompted the use of skeleton photoperiods on *Megoura* to test the hypothesis that photoperiodic timing in this aphid is effected by an endogenous circadian rhythm with properties similar to those of *Drosophila* and *Lemna*. The opposing hypothesis, based on earlier work with *Megoura*, is that there is a non-rhythmic timer that simply measures each dark period. Similar skeleton photoperiod experiments have been reported with *Pectinophora* but the light periods used were apparently too short to affect the photoperiodic response at all[7].

Lees's clone of *Megoura viciae* Buckton was used, with frequent transfer to fresh seedlings of a dwarf *Vicia faba* to avoid crowding and thus ensure that all females were apterae (wingless). Stock cultures were raised at approximately 15° C under continuous cool, white fluorescent light of about 1,000 L, a condition in which all females produced are virginoparae, producing only embryos rather than ova. The same temperature and light intensity were used for the experimental treatments.

I began by transferring several fourth instar apterae from the stock conditions to those being tested, where they produced abundantly the offspring which were the actual individuals under treatment. The original apterae were generally discarded after 7 days, and after a further 7 days, 21 individuals from each treatment were removed to ordinary room conditions and segregated in such a way that their subsequent offspring could be collected and identified. Approximately two weeks later, the families of offspring produced by each individual were preserved in 25% ethanol containing 1 g⁻¹ phenylthiourea. Ten of the largest (oldest) in each family were later examined to determine whether they were virginoparae or oviparae.

Results are presented as the percentage (VP%) of treated individuals from a total of 18 to 21, depending upon mortality, whose ten largest offspring include five or more virginoparae. In preliminary experiments, VP% was 100 when the 14-day treatment was entirely under continuous light; VP% was 0 when the entire 14 days was under a schedule of 11(13), (11 h light, 13 h darkness) and VP% was 40 with 14 1/4 (9 3/4), and also with first 7 days under 11(13) and the next 7 under continuous light. These results agree closely with those previously reported[3,4,8].

Results and the relative values expected within each pair or group of treatments on the ECR hypothesis are summarized in Table 1. These expectations were never fulfilled. For experiments A to D to support the ECR hypothesis and conform to results with *Lemna* and *Drosophila*, the expectations were that the schedule 1(9)1(13), started immediately following continuous light, should have a long-day effect, as if the 9-h dark period were being read as the night phase; 1(13)1(9), under the same circumstances, should have a short-day effect, with the 13-h dark period read as night phase; and an initial 12 h of darkness should convert each such result to its opposite by displacing the phase relationship by half a circadian cycle[2,6]. Only saturatingly high long-day effects, however, were obtained in all four treatments.

There are two possible objections to these experiments. First, the *Lemna* work suggests that the differences sought might well be unstable, occurring during the first few days but easily obscured in a two week treatment[6,9]. In *Lemna*, such instability results in the short-day and not the long-day effect, but the reverse might occur in *Megoura*. Second, even stable but small differences in the potential action of treatments could be obscured by continuing the exposure to saturation. I therefore undertook experiments E to G in which two of the schedules used previously were given as 7-day pretreatments to an unambiguously short-day schedule 12(12), in order to produce intermediate VP% values. Both pretreatments also had approximately the same effect which disagrees with the ECR hypothesis. Even if the small difference should prove statistically significant or survive a longer series of experiments, it would be in the opposite direction. Such a result would precisely accord with the non-circadian hypothesis, as there is one more short (9 h) night in the schedule giving the higher values[4].

The experiments A to G depend upon the assumption that the two dark periods in 1(9)1(13) and 1(13)1(9) are sufficiently similar so that for a circadian system, the schedules are ambiguous and effects thus depend on the initial dark period. The decisively long-day effects obtained, however, made it necessary to modify the schedules to increase the probability of a short-day response. Changing a previously long-day schedule should at some point result in ambiguity if the ECR hypothesis is correct. On this hypothesis, further reducing the length of the shorter dark period should increase the likelihood of the longer one being read

Table 1 Photoperiodic Response of. *Megoura viciae* to Skeleton Photoperiods, and Expectations on the Endogenous Circadian Rhythm (ECR) Hypothesis

Experiments	Light (dark) schedule (h) Day 1	Days 2–7	Days 8–14	Virginopara-producers; percentages and means		ECR expectations
A–C	1(9)1(13) ⎫	1(9)1(13)	⟶	100, 100, 100:	100	High
A–C	12(12) ⎭			100, 100, 100:	100	Low
A, B, D, E	1(13)1(9) ⎫	1(13)1(9)	⟶	100, 100, 100, 100:	100	Low
A, B, D, E	12(12) ⎭			100, 100, 100, 100:	100	High
E–G	1(13)1(9) ⎫	1(13)1(9)	12(12)	76, 43, 55:	58	Low
E–G	12(12) ⎭			62, 38, 40:	47	High
H–J	4(3)3(13) ⎫	4(3)4(13)	⟶	0, 0, 0:	0	High
H–J	11(13) ⎭			0, 0, 0:	0	Low
H, I, K, M–O	3(5)3(13) ⎫	3(5)3(13)	⟶	10, 30, 20, 30, 5, 20:	19	High
H, I, K	11(13) ⎭			25, 15, 15:	18	Low
M–O	3(13)3(5)	⟶	⟶	15, 17, 15:	16	Low
L–O	2(7)2(13)	⟶	⟶	90, 90, 70, 95:	8y	High
L–O	2(13)2(7)	⟶	⟶	90, 95, 75, 90:	88	Low

as the night phase, and so schedules 4(3)4(13), 3(5)3(13) and 2(7)2(13) were tested. These schedules should also have an increased short-day tendency on the non-circadian mechanism because light-interruptions are minimally effective in *Megoura* after about 4 h of darkness, and earlier interruptions only reset the dark period timer to its starting condition[3,4]. Increased short-day tendency (resulting in ambiguity) should, under the circadian hypothesis, increase the susceptibility of the effect to inversion by an initial 12- or 13-h dark period. The non-circadian hypothesis does not require this prediction. Effects expected on the basis of the ECR hypothesis were not to be found (Table 1).

Lees concluded that *Megoura* photoperiodism does not involve an endogenous circadian rhythm on the basis of experiments with long dark periods and with light/dark cycles of various lengths[3,4]. The first type of experiment depends on the assumption that a circadian oscillation would persist through the dark periods, while the second assumes that such a timer would be severely limited in its capacity to entrain to non-circadian periodicities. There are some rhythms, as for example[5,6] in *Lemna*, that persists only very weakly without external signals, and even the highly persistent rhythm of carbon dioxide output in *Bryophyllum* cannot be entrained to a 6-h periodicity[10]. Neither persistence beyond one cycle nor resistance to non-circadian periodicities, whatever their value to other processes, has any obvious role in a photoperiodic timer, and it would not be surprising to find one in which both characteristics had been lost. If such a timer had originated in a more typical ECR system, and still retained some of its basic features, these features might be revealed under skeleton photoperiods as these supply repeated 24-h signals while examining the response to other inputs.

None of the effects of skeleton photoperiods on *Megoura* resemble those with *Lemna* or *Drosophila* and all can be accounted for by the non-circadian scheme proposed by Lees[3,4], this is overwhelming evidence against even a rudimentary form of circadian timing in *Megoura* photoperiodism. The attractive concept of one universal timing mechanism in photoperiodism seems thus even more difficult to maintain.

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Batesian Mimicry between *Danaus chrysippus* and *Hypolimnas misippus* (Lepidoptera) in Tanzania

Danaus chrysippus (Danaidae) is a common butterfly of open country throughout tropical Africa[1]. The species is reputed to be distasteful and there is experimental evidence of this for a related American species, *D. plexippus*, in which the associated warning coloration has also been shown to be effective against predators[2,3]. *D. chrysippus*, which also shows warning coloration, is strikingly polymorphic over much of its range and four sympatric forms have been described from Uganda[1]. It acts as
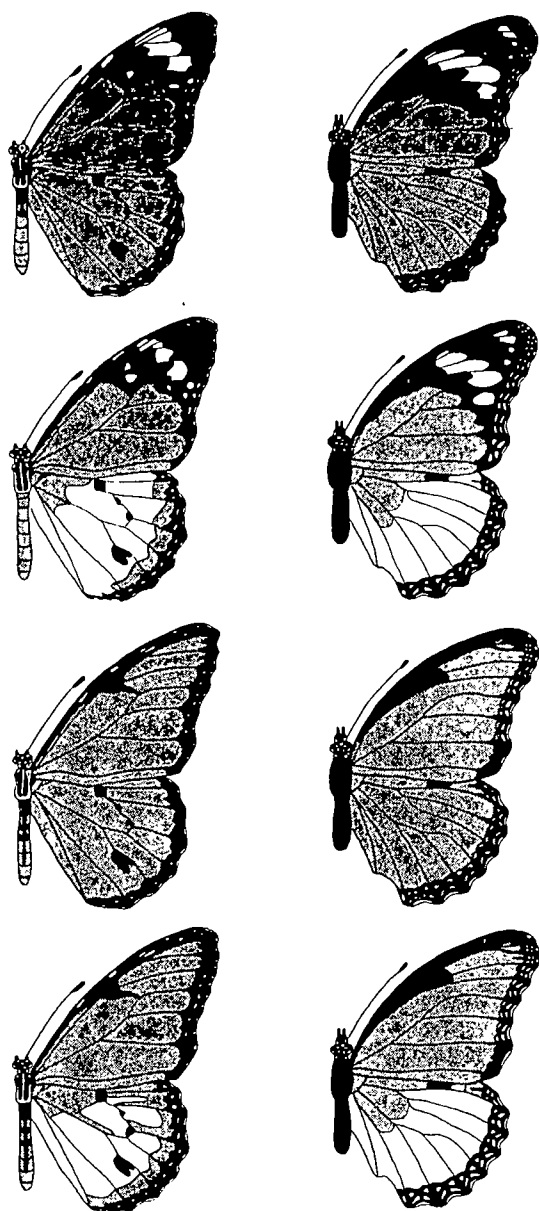
Fig. 1 The four colour forms of *Danaus chrysippus* (left) and the corresponding female forms of *Hypolimnas misippus*. The forms of *D. chrysippus*, in order from the top, are named *chrysippus*, *alcippus*, *dorippus*, and *albinus*. The corresponding forms of *H. misippus* are *misippus*, *alcippoides*, *inaria* and *inaria-alcippoides*. The black and white areas in the figure are black and white as shown and the shaded area is orange. The male of *H. misippus* is black and white and quite different from any of the female forms (from ref. 6).

a model for several mimetic butterflies and is commonly involved in a supposed Batesian complex with *Hypolimnas misippus* (Nymphalidae) of which there are also four distinct female morphs[4-6], each resembling closely a morph of *D. chrysippus*. (Male *H. misippus* are monomorphic, black and white and not mimetic.) There has been some doubt, however, about the efficiency of the mimicry as some morphs of *H. misippus* may be common in the absence of their *D. chrysippus* models. Also the abundance of the edible mimic is sometimes greatly in excess of that of the model[6], which does not conform to what would normally be expected from Batesian mimicry theory[6,7].

My study is based on regular sampling for both *D. chrysippus* and *H. misippus* in rough grassland on the campus of the University of Dar es Salaam, Tanzania. All four described morphs of both species (Fig. 1) are present, though some are rare. Intermediate forms of *H. misippus* with respect to both

forewing and hindwing coloration occur and no individual with a fully developed white hindwing patch was seen. Six forms are therefore scored; all *alcippoides* and *inaria-alcippoides* were animals with some white on the hindwing but not the full white patch. The results of five months' sampling are shown in Table 1.

Table 1 Distribution of Female Morphs in *Hypolimnas misippus**

Hindwing	Morph	Number examined	% frequency of ♀ morphs
Plain orange	*misippus*	15	34.1
	transitional forewing	6	13.6
	inaria	16	36.4
Orange with white patch	*alcippoides*	3	6.8
	transitional forewing	3	6.8
	inaria-alcippoides	1	2.3
	Total	44	100.0

* Collected between February and June 1972 at Dar es Salaam.

The frequency of the four morphs of *D. chrysippus* over the same period is given in Table 2. The forms scored as *alcippus* and *albinus* did not have a fully developed white patch and may be heterozygotes[1].

D. chrysippus (309 caught) was much more abundant than *H. misippus* (99 caught, 44 female and 55 male) as expected[6]. If the palatable mimic approaches or exceeds its model in abundance, predators will probably quickly learn to recognize a phaneric pattern associated with palatability and the safety of both mimic and model is threatened. The relationship gives selective advantage only when the mimic is relatively rare. There is experimental evidence[2,3] that birds will eat warningly coloured edible mimics if they have not had previous experience of the distasteful model.

Table 2 Distribution of Morphs in *Danaus chrysippus**

Morph	Number examined	% frequency
chrysippus	132	42.7
dorippus	171	55.3
alcippus	4	1.3
albinus	2	0.7
Total	309	100.0

* Collected between February and June 1972 at Dar es Salaam.

Because *H. misippus* is a fast flying butterfly and not as easy to catch as *D. chrysippus*, the comparative numbers of the two species caught may not be indicative of their true proportions. Female *H. misippus*, however, amount to 14.3% of the *D. chrysippus* (both sexes) caught and this figure is close to other estimates of the ratio of mimic to model[6,8] in tropical mimetic assemblages.

This investigation is the first where all four forms of both species are sympatric. The figures given in Tables 1 and 2 show that the frequencies of the four forms of the mimic are similarly ranked to the corresponding forms of the model (the forms of *H. misippus* with a transitional forewing are omitted from the ranking). The probability of such a ranking is 1/24 and is therefore statistically significant at the 5% level. This result suggests that mimetic resemblance is an important factor influencing natural selection in *H. misippus*. Heterosis has been postulated to explain the existence of forms of the mimic where the corresponding model is absent[7], as in Ghana and India, but is unnecessary for the populations described here.

While mimetic resemblance is sufficient to explain the polymorphism in *H. misippus*, it does not account for that of the model. *D. chrysippus* is involved in a Müllerian mimetic assemblage with another distasteful butterfly, *Acrea encedon*

(Acraeidae) in the region of Dar es Salaam as in other parts of Africa[9], and is also mimicked by other species. It has been suggested[1] that the polymorphism of *D. chrysippus* is a means of breaking down to some extent the resemblance of mimics to the model, as the model will have a selective disadvantage if it has too many mimics.

My results are in agreement with the classical mimicry theory that the mimic is much less abundant than its model and the frequencies of the four morphs are identically ranked in the two species.

Further results will be published elsewhere.

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Negative Non-random Mating in the Polymorphic Butterfly *Danaus chrysippus* in Tanzania

FOUR distinct morphs of the common savannah butterfly *Danaus chrysippus* are found in the region of Dar es Salaam, Tanzania. These forms have been described[1] and their relative frequencies on the campus of the University of Dar es Salaam during 5 months of sampling are known[2]. The *dorippus* and *chrysippus* forms are relatively common while *alcippus* and *albinus* are both rare.

Table 1 Sex Ratios in a Population of *Danaus chrysippus* between February and July 1972

Month	Number examined	*dorippus* %♀	%♂	χ^2	*chrysippus* %♀	%♂	χ^2
Feb.	26	68.4	31.6	2.58	42.9	57.1	—*
Mar.	28	47.4	52.6	0.05	33.3	66.7	—*
Apr.	51	56.2	43.8	0.50	57.9	42.1	0.47
May	81	27.3	72.7	9.09†	45.9	54.1	0.24
June	117	26.3	73.7	12.79‡	40.0	60.0	2.40
July	123	26.5	73.5	15.06†	43.6	56.4	1.47

* Sample too small to calculate χ^2. † $P<0.01$, ‡ $P<0.001$.

To calculate the frequencies of pairings expected as a result of random mating it has not been possible to assume a 1:1 sex ratio throughout the sampling period. The results indicate that the sex ratio, particularly in form *dorippus*, is far from constant. Monthly sampling figures from February to July 1972 are given in Table 1. Highly significant departures from a 1:1 sex ratio are apparent in the *dorippus* form from May to July when there is an excess of males over females. None of the values of χ^2 for the sex ratio in *chrysippus* shows a significant departure from a 1:1 expectation. It has been pointed out[1] that the sex ratios of samples taken in the field may not be an accurate reflexion of the true sex ratio because males are more

active than females and therefore more liable to be caught. The type of activity also influences the results, males being commoner in samples taken while feeding at flowers and females predominating during egg laying activity. The lack of departure, however, from the expected 1:1 ratio in form *chrysippus* throughout and in form *dorippus* from February to April, suggests that the departure from a 1:1 ratio in *dorippus* from May to July is a real one. An alternative possibility is a change in the behaviour of *dorippus* males which renders them more liable to capture, but this is unlikely since the ratio of *dorippus* males to *chrysippus* males over the whole period has been constant ($\chi^2_{(5)}=1.49$; $0.95>P>0.90$), while the corresponding ratio for females changed greatly over the same period ($\chi^2_{(5)}=14.65$; $0.02>P>0.01$) (Table 2). Consequently, expected values for the frequencies of pairings assuming random mating, have been made on a monthly basis using the observed sex ratios in each sample.

Records of mating frequencies in the field are available for all 6 months during which 31 mating pairs have been seen. Results are given for the *dorippus* and *chrysippus* forms only, as the rare *alcippus* and *albinus* forms were not seen mating. The observed and expected frequencies of pairings assuming random mating are given in Table 3. The value of χ^2 based on the four possible matings is statistically significant at the 5% level and a comparison of like with unlike matings gives a more significant value ($\chi^2_{(1)}\doteq6.33$; $0.02>P>0.01$).

Table 2 Morph Ratios in a Population of *Danaus chrysippus** between February and July 1972

Month	Number examined	Males *dorippus*	*chrysippus*	Females *dorippus*	*chrysippus*
Feb.	26	60.0	40.0	81.3	18.7
Mar.	28	62.5	37.5	75.0	25.0
Apr.	51	63.6	36.4	62.1	37.9
May	81	61.5	38.5	41.4	58.6
June	117	53.8	46.2	38.5	61.5
July	123	61.7	38.3	42.9	57.1

* Small numbers of the morphs *alcippus* and *albinus* are omitted from the table.

Table 3 Frequencies of Observed Matings in a Population of *Danaus chrysippus*

Month	*dorippus* ♂ X *dorippus* ♀	*dorippus* ♂ X *chrysippus* ♀	*chrysippus* ♂ X *dorippus* ♀	*chrysippus* ♂ X *chrysippus* ♀
Feb.	2 (1.96)	0 (0.45)	2 (1.30)	0 (0.30)
Mar.	2 (1.41)	1 (0.28)	0 (0.84)	0 (0.47)
Apr.	0 (1.58)	2 (0.96)	2 (0.90)	0 (0.55)
May	1 (1.53)	1 (2.16)	3 (0.95)	1 (1.16)
June	0 (1.45)	3 (2.32)	2 (1.25)	2 (1.99)
July	1 (1.86)	3 (2.46)	3 (1.15)	0 (1.53)
Total	6 (9.79)	10 (8.63)	12 (6.39)	3 (6.20)
χ^2	1.467	0.217	4.925	1.652

$$\Sigma\chi^2_{(3)}=8.261; 0.05>P>0.02.$$

Expected frequencies assuming random mate selection in parentheses.

Observations so far suggest that two mechanisms exist in this population which would be expected to perpetuate a polymorphism. First, negative non-random mating occurs in which the *chrysippus* form is more likely to mate with *dorippus* than with its kind. This is particularly so for matings between *chrysippus* males and *dorippus* females which are much more numerous than expected. This effect is not the result of differential success in mating by either sex of either morph. Both sexes and morphs are involved in mating pairs in the proportions expected from the composition of the population ($\chi^2_{(1)}$ for males $=0.329$; $0.80>P>0.50$: $\chi^2_{(1)}$ for females $=0.147$; $0.80>P>0.50$). Second, the excess of the *dorippus* form among males and *chrysippus* among females between May and July (Table 2),

which has been allowed for in calculating random expectations, must contribute independently to the maintenance of the polymorphism, because each is more likely to encounter the other morph in searching for a mate. The mechanism responsible for the unequal sex ratio in *dorippus* is not yet clear, but it seems that the phenomenon may be seasonal. It is hoped that further observations will clarify this.

Non-random mating has not been reported often in Lepidoptera although it has long been known in the arctiid moth, *Panaxia dominula*[3] where it is responsible for the maintenance of the *medionigra* gene in the population.

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Fig. 2 *H. proavus*, same as Fig. 1. (Scale=1 µm.)

Marine and Freshwater Skaters: Differences in Surface Fine Structures

TRACHAETE arthropods, notably insects, are almost totally absent from the open ocean for various reasons which are still largely speculative[1-3]. *Halobates* (Heteroptera) is an exceptional insect genus which is exclusively marine, with several open-ocean species that spend their entire lives thousands of miles away from land. It is a member of the family Gerridae, which includes the common pond-skaters or water-striders. Although species of *Halobates* have been known for more than 150 yr, there is little information about their biology and about specific adaptations which might enable them to live in the oceans where all other insects have failed[4].

Some of the special adaptive features of *Halobates* that may be involved in the conquest of their unusual habitat probably lie in the body surface, and we examined surface fine structures of *Halobates germanus* White, from the central Pacific Ocean, and *H. proavus* White, from the Malayan coast. A related

Fig. 3 *H. germanus*, lateral view of section of mesothorax showing microtrichia. (Scale=1 µm.)

freshwater *Ventidius* species of the same subfamily (Halobatinae) was also studied for comparison.

All the scanning electron micrographs shown here are of dorsal thoracic surfaces. Figs. 1 to 3 are of *Halobates* (surface fine structures of the two species studied were similar) and Figs. 4 and 5 are of *Ventidius*. In both genera, "pits" or "depressions" are found on the head and thorax, being more abundant on the sides than in the middle. Surface fine structures of the dorsal abdominal region are very similar to those of the thorax, although there are fewer pits; none have been found on the ventral surface.

The most striking difference between the two genera is in the shape of the microtrichia forming, presumably, the plastron, a thin film of gas supported by a layer of fine hairs which are set sufficiently close together to be resistant to wetting. The plastron serves to provide and maintain enough oxygen to satisfy the respiratory requirement of a submerged insect[5]. In *Ventidius* the microtrichia are simple pegs (Fig. 5) about 1 µm high, 0.3 µm wide at the base, and spaced 0.5 µm apart. In *Halobates* they appear from the top view like mushrooms, but from the side they are revealed to be thick hooks with the tips bent at about 90° (Fig. 3). These hook-like structures are about 1.5 µm high, 1.0 µm wide across the top, 0.5 µm wide at the base, and spaced 1.5 µm apart, the average "inter-

Fig. 1 *Halobates proavus*, dorso-lateral region of mesothorax showing hairs, pits, and mushroom-like microtrichia. (Scale= 10 µm.)
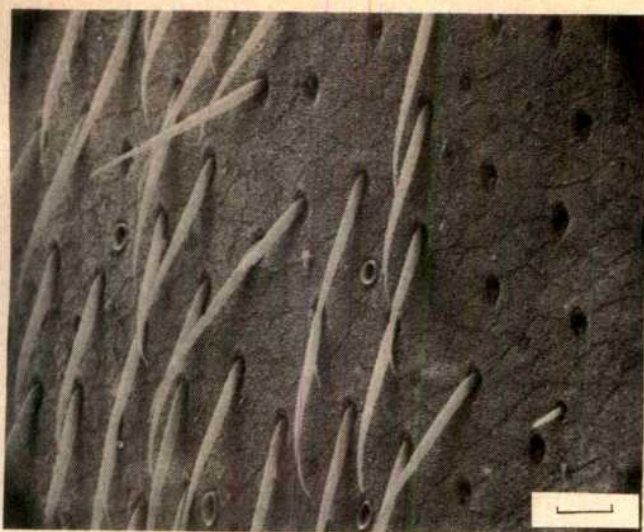
Fig. 4 *Ventidius* species; dorso-lateral region of mesothorax showing hairs, hair base, pits, and velvety mat of microtrichia. (Scale = 10 μm.)
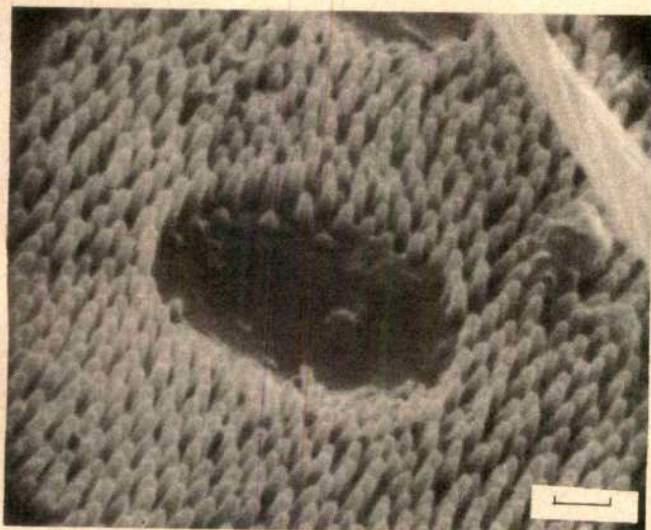
Fig. 5 *Ventidius* sp.: Same as in Fig. 4, showing pit and peg-like microtrichia. (Scale = 1 μm.)

cap" distance being 0.5 μm. They are quite unlike the plastron of certain intertidal flies (Diptera) studied by Hinton[6,7]. According to Thorpe and Crisp[8], such an arrangement of bent hairs, as seen in *Halobates*, can be expected to form a more efficient plastron than a velvety layer of straight hairs.

The evident differences in surface fine structures between marine and freshwater skaters may be expected to have some biological or ecological significance. Species of *Ventidius*, which normally skate on the surface of running water in tropical streams, presumably sometimes need to dive (as has been observed for *Gerris* sp.) to lay eggs on submerged objects and would therefore be expected to have developed less water repellent surfaces, which would permit their occasional submergence. On the other hand, *Halobates* sp., being restricted to the ocean surface, without protection from rain, spray or waves, would presumably require their surfaces to be as water-repellent as possible in order to minimize the danger of drowning during periods of accidental submergence. They might therefore be expected to have developed a highly efficient plastron, as well as a markedly hydrofuge body covering. These features

would not be expected to handicap them during oviposition, as they lay their eggs exclusively on flotsam[4].

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Acceleration by Ecdysterone of Premoult Substages in the Crayfish

AN insect does not enter premoult if its thoracic glands have been removed, nor a crustacean if its y-organs have been removed, but once premoult is under way it continues whether or not the glands are present[1,2]. This suggests that the hormone secreted by these glands acts merely as a trigger to initiate premoult, and as the injection of ecdysone also initiates premoult, this is the hormone thought to be secreted. Also, the brain-ring gland complex of *Calliphora*, which contains the homologues of the thoracic glands, has been shown to produce substances similar to ecdysone and crustecdysone[3].

If ecdysone acts only as a trigger, then injections of ecdysone should have no effect on any stages of premoult development except the initial stage. Consistent with the trigger hypothesis, ecdysone produces an effect on insect pupal development only if injected early enough[4]. Ecdysone, however, is known to affect many diverse processes most of which are not restricted to early premoult, such as dopa decarboxylase synthesis[5], conversion of glucose to trehalose[6], cell movement[7,8], calcification[9], apolysis[10,11], formation of gastroliths[12], and many more. Levels of ecdysone rise and fall during the moult cycle[13-17], which also suggests that the hormone has separate control functions over different processes during the cycle. Furthermore, the effects of ecdysone vary according to the amount present; for example, Rao (personal communication) found that the injection of 5 μg of ecdysterone per animal into fiddler crabs caused apolysis but not moulting. Others found that the time required to initiate premoult after ecdysterone injection into crayfish varied inversely with the dose[11], while injected ecdysterone speeded the mount of animals already in premoult at the injection time[18], and crayfish induced to enter premoult by eyestalk removal moulted sooner if injected with ecdysterone[12,19]. Ohtake, Milkman and Williams[20] found evidence for a covert accumulation of the effect of ecdysone on the tissues. Thus, ecdysone does not produce a single event, but an accumulative series of events as hormone secretion continues over a span of time.

Ecdysone stimulates the production of additional ecdysone[15], a positive feedback system, which may explain how ecdysone can serve both as a trigger and controller. Thus, an injection of ecdysone may stimulate the production of sufficient hormone to produce all the changes necessary for moulting. The thoracic glands or y-organs need not be present for this response because other organs are capable of ecdysone synthesis, as shown by the fact that isolated abdomens of the silkworm *Bombyx* convert labelled cholesterol into ecdysone[21].

Little is known about the effects of ecdysone in crustaceans. How early in premoult must ecdysone be injected in order to have an effect? Does ecdysone stimulate events in every stage

of premoult or only in some? Can the progression from each premoult stage to the next be speeded by ecdysone? Our investigation was designed to answer these questions.

Specimens of *Orconectes sanborni* were collected in a stream near Kent, Ohio, and maintained in the laboratory, each in a separate, partitioned cubicle of an acrylic plastic aquarium containing tap water recirculating through calcareous gravel. Each experimental animal was matched with a control animal of the same sex, weight, and moulting stage; only crayfish in intermoult and premoult stages were used. Experimentals were injected with 2 µg g^{-1} body weight of ecdysterone (Mann Research Laboratories) dissolved in Van Harreveld[22] solution at a concentration of 2 µg per 10 µl., and controls were injected with the same quantity of Van Harreveld solution alone. After injection, the moulting stage of each animal was determined as described by Stevenson[23-25] at 24 h intervals for at least seven days. Animals were randomly assigned to compartments and identified by code so that the group and past history of an animal would not be known at the time of staging.

Table 1 Injection of Ecdysterone into Crayfish at Various Moulting Stages

Initial moulting stage	Mean difference, in days	p less than:	n*	$s_{\bar{x}}$†	t‡
C_{3-4}	2.56	0.0005	9	0.34	7.53
D_0	6.9	0.0005	10	0.71	9.71
D_1'	2.5	0.0005	10	0.43	5.81
D_1''	1.17	0.05	6	0.48	2.44
D_2	1.5	0.005	8	0.42	3.57

* Number of pairs in each group.
† Standard error of difference.
‡ Student's t test.

In the case of every moulting stage studied, the crayfish injected with ecdysterone entered the next succeeding moulting stage significantly sooner than those injected with the Van Harreveld solution alone. Table 1 shows the moulting stage of each group at the time of injection, the mean difference between the number of days required by each experimental animal to enter the next succeeding mounting stage and the number of days required by the corresponding matched control animal, and the probability of such a difference occurring by chance according to a one-tailed Student's t test. The table also shows the number of pairs in each group (n), the standard error of the difference $s_{\bar{x}}$ and t. Every value of P was below 0.05, and most were much lower.

These results show that ecdysterone not only causes the initiation of premoult, but continues, during the premoult stages studied, to stimulate the various processes that prepare the animal for the next moult.

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A Salamander Midwife

J. P. A. ANGSEESING[1] is mistaken in most of his criticism of Kammerer's experiments as described by Koestler[2]. Angseesing quite reasonably supposes that the formation of nuptial pads on male midwife toads might involve a genetic mechanism activated by their confinement to aquatic conditions or high temperature. The crux of the argument, however, is the claim that this condition was inherited and intensified in successive generations. Any explanation must therefore involve selection or the inheritance of acquired characteristics, in addition to the probable physiological mechanism.

Contrary to Angseesing's assertions, the colour of newborn salamanders shows no detectable maternal effect, is quite unlike the colour of either parent, and is not likely to be varied by maternal hormones. I have assisted at the delivery of *Salamandra maculosa*, with which Kammerer worked, and so can claim to be a salamander midwife. The embryo of ovoviviparous races develops in an exceptionally stable environment: within a jelly capsule in the uterus of an animal which is hibernating underground, and so relatively unaffected by fluctuations of light and temperature. Even if the appropriate maternal hormones were able to penetrate these barriers to the embryo, which is not known, it seems probable that the amounts of hormone would be remarkably uniform in all cases. Escaping from its capsule within a few minutes of birth, the larva has a mottled grey-brown coloration. It only acquires the brilliant orange-gold and black pattern at metamorphosis, weeks or months later. Kammerer considered that the background caused a corresponding inherited change in the adult pigmentation. Anyone familiar with the variety of adult colour patterns in these salamanders would realize that he could only demonstrate the point by starting with pure-breeding lines, in order to prevent inadvertent selection or genetic assimilation[3].

A Lamarckian explanation of these experiments would clearly be important, as indicating a directed mechanism of evolution (and of genetic engineering) which has been generally discounted. The obvious bias in Koestler's book[2,4] cannot disguise the fact that Kammerer's evidence was inadequate and in one case forged, and therefore discredited. The conception of the experiments, however, was more precise than Angseesing allows. Those of us who cannot read German should be grateful to Koestler, even if we cannot agree with his conclusions.

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Elevated Arterial Blood Pressure in an Asymptotic Population of Meadow Voles (*Microtus pennsylvanicus*)

THE factors regulating the growth and final size of mammalian populations include climatic conditions, availability of food, predation, disease, and intraspecific strife[1-3]. In studies of the demography and organ weight changes in increasing animal numbers in freely growing confined populations of mice, Christian, Lloyd and Davis[4] have observed that the population growth curve will reach an asymptote after which the population remains close to this size. The attainment of the upper asymptote is associated with cessation of rearing of all young animals. It is not known why reproduction fails at high density but it may involve behavioural changes, failure of lactation and increased intrauterine mortality.

There are many data on the growth rates and organ weights of confined populations but little is known about the physiological status of these animals. In this study a population of meadow voles (*Microtus pennsylvanicus*) was

Table 1 Measurements of Animals from a Freely Growing Confined Population and Caged as Bisexual Pairs

| | | Population | | | | Bisexual pairs | | |
| | | Body | Blood | | | Body | Blood |
Sex	Age*	weight†	pressure‡	Sex	Age*	weight†	pressure‡
M	374	53	120	M	482	46	120
F	374	50	120	F	449	40	112
M	308	64	122	F	378	36	105
F	240	43	110	F	377	39	98
F	195	68	120	M	295	64	112
F	195	69	115	F	293	32	115
F	195	62	117	F	278	44	90
M	178	71	122	M	242	46	122
M	178	51	117	F	220	37	102
F	178	54	125	F	196	36	98
F	178	42	135	F	196	42	110
M	85	55	133	F	161	59	105
F	85	50	120	M	158	42	112
M	85	36	123	M	140	27	100
				F	118	54	95
				M	116	52	115
				F	116	24	120
			$\bar{x}$ 121				$\bar{x}$ 107

* In days. † In g. ‡ In mm Hg.

allowed to reach its asymptotic density and arterial blood pressure was measured. Animals caged as bisexual pairs served as controls.

The population was housed in a stainless steel cage divided into two communicating levels each measuring 2×4.5 foot. Litter material included wood shavings and newspaper placed in the cage at the start of the experiment and not changed, and metal cans were provided as nest sites. Excess food and water were provided, and the lighting, temperature and humidity were controlled. The population was started by introducing one male and two female weanling voles into the cage and leaving them undisturbed except for a monthly census. The population was allowed to grow until reproduction ceased as indicated by a lack

of new animals present after three consecutive months. The voles were anaesthetized with urethane (1 g kg⁻¹), a carotid artery cannulated with polyethylene tubing (PE 10) and the mean arterial pressure recorded with a 'Statham' strain gauge and 'Gilson' recorder. If any blood loss occurred or the cannula was not patent, the data were not included in the results. Organ weights were determined after fixation in 10% neutral buffered formalin. Animals of approximately the same age distribution, caged as breeding pairs, were used as controls for the animals from the freely growing population, and their blood pressure was measured identically.

The population was terminated after 354 day; the last litter from which any animals survived beyond weaning was born at 270 day. At sacrifice there were twenty-two voles present of which twelve were females and ten were males. Of the females, seven were pregnant but four had resorbing embryos.

Measurement of the blood pressure was successful in fourteen of the twenty-two population animals and seventeen of the twenty control animals. The mean blood pressure of the population was 121 ± 1.7 (s.e.m.) mm Hg while that from the control animals was 107 ± 2.3. By Student's t test for group comparisons, this difference is very highly significant with $P < 0.001$. The only significant difference between organ weights observed was that the thymus glands of animals from the population were smaller (0.42 ± 0.05 mg g⁻¹ body wt) when compared to the control animals (0.90 ± 0.10) ($P < 0.001$).

Bernardis and Skelton[5] reported that rats with adrenal regeneration hypertension showed greater increases of blood pressure when housed three per cage as compared to singly caged rats. Henry *et al.*[6] observed raised blood pressure in crowded mice and these workers, as well as others[7,8], have pointed out that social pressures or stress may be involved in the genesis of essential hypertension. My study shows that when animals are allowed to interact until they reach a high stable population density they demonstrate a small, but consistent, elevation in blood pressure. There is evidence that cessation of reproduction may be associated with an altered state of the pituitary-adrenal-gonadal system[4], and many investigators have also demonstrated a relationship between adrenal steroids and hypertension[9].

Because thymic involution is a recognized indication of increased adrenocortical function, I suggest that the occurrence of hypertension in asymptotic populations might also be a function of increased adrenocortical function.

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The Ancestry of Birds

WALKER[1] has restated the long-held belief that both birds and crocodiles evolved from thecodont ancestors, but he added the novel suggestion that these two groups arose from a common thecodont ancestor and thus are much more closely related than has been previously realized. Inasmuch as the Thecodontia include the most primitive as well as the most ancient archosaurs known, it is highly probable that all subsequent archosaurs (including birds) were derived from members of this order. Although Walker may be correct, I do not think that the evidence cited indicates such a close relationship between birds and crocodiles as he proposes.

My purpose here, however, is not to challenge Walker's evidence or his interpretation of it. Rather, it is to present (in summary form) other evidence pertaining to the immediate (as opposed to the remote) ancestry of birds—evidence which has generally been ignored for the past 50 years.

The critical evidence of bird ancestry is preserved in the four presently known specimens of Archaeopteryx, which occupy a position much closer to avian origins than do the Triassic thecodonts mentioned by Walker. Before we can trace the remote origin of birds among thecodonts, we must be certain that we have correctly assessed the evidence in those specimens pertaining to the immediate ancestors of Archaeopteryx. With this in mind, during the past two years, I have studied all four Archaeopteryx specimens and currently I am preparing a detailed paper on the origin of birds. Walker's paper, however, has prompted this preliminary note, for in my opinion his theory can only be valid if it is totally consistent with a thecodont–coelurosaur–Archaeopteryx–Aves phylogeny. The skeletal anatomy of Archaeopteryx is almost entirely that of a coelurosaurian dinosaur—not thecodont, not crocodilian, and not avian.

The following coelurosaurian features of Archaeopteryx collectively are here considered as prima facie evidence of a coelurosaurian (Theropoda) ancestry of birds:

(a) Vertebral column: (1) Thoracic vertebrae pleurocoelous (and probably amphicoelous). (2) Ten cervical vertebrae and 12 to 15? thoracics.

(b) Fore limb: (3) Manus reduced to digits, I, II and III. (4) Phalangeal proportion of the fingers. (5) Proportions of the three metacarpals. (6) Carpus of two or three elements including a lunate radiale. (7) Proportions of humerus to radius and ulna. (The fore limb is not reduced in all theropods as has been frequently claimed; see for example Ornitholestes, Velociraptor, Deinonychus, Ornithomimus and Deinocheirus.) (8) Morphology of the humerus.

(c) Pectoral arch: (9) Very narrow, strap-like scapula. (10) Subrectangular coracoid fused to scapula.

(d) Hind limb: (11) Pes with four digits, V being lost. (12) Phalangeal proportions. (13) Reversed hallux. (14) Metatarsal proportions. (15) Mesotarsal joint. (16) Well developed ascending process of the astragalus. (17) Hind limb proportions. (18) Morphology of the femur.

(e) Pelvis: (19) Shape of the ilium. (20) Shape of the pubis, with a distal expansion and a long symphysis. (21) Open acetabulum.

In addition, it is possible that the pubis of the Berlin specimen (apparently preserved in the avian position) is dislocated and that it was originally directed ventrally or antero-ventrally as in theropods[2]. The proximal portion of that pubis is damaged, and the pubis of the Teyler specimen is oriented nearly perpendicular to the axis of the posterior thoracic vertebrae rather than obliquely as in the Berlin specimen.

Certain other non-avian characters present in Archaeopteryx, although perhaps primitive in origin are also typical of coelurosaurs. These are: (1) Long, unfused caudal series numbering at least 20 segments and apparently with elongated zygapophyses and chevrons. (2) Presence of gastralia. (3) Thecodont dentition. (4) Antorbital fenestra. (5) Probable presence of an external mandibular fenestra.

Many of these characters have been noted before, but two very important features have not. First, the lunate form of the radiale in Archaeopteryx has only recently been recognized in theropods (namely Deinonychus[3], Stenonychosaurus[4] and a recently collected specimen probably referable to Velociraptor (Kielan-Jaworowska, personal communication)). Second, the astragalus in Archaeopteryx has a well developed ascending process that apparently has not been noticed before, even though it is conspicuous in both the London and Berlin specimens.

These "coelurosaurian" characters of Archaeopteryx have in the past been attributed to parallel or convergent evolution, but the large number of features involved, and the complex nature of many of them, make this highly improbable. In my opinion, common ancestry alone cannot account for the overall coelurosaurian nature of Archaeopteryx.

No one any longer doubts the avian identification of these specimens—or their significance for the origin of birds, presumably because of the remarkable feather impressions. Yet they possess only two osteological characters that are exclusively avian, the furcula (preserved in the London and Maxberg specimens) and the possibly reverted pubis (doubtfully preserved in natural articulation only in the Berlin specimen). Indeed, if feather impressions had not been preserved all Archaeopteryx specimens would have been identified as coelurosaurian dinosaurs. The only reasonable conclusion is that Archaeopteryx must have been derived from an early or mid-Jurassic theropod.

A dinosaurian origin of birds is not a new idea, but it has been widely dismissed for the last 50 years because Broom[5] and Heilmann[6] concluded that coelurosaurs were not sufficiently primitive. The sole anatomical evidence cited by Heilmann for rejecting a coelurosaurian ancestry for Archaeopteryx was the absence of clavicles in all known theropods. Clavicles have been reported, however, by Camp[7] in Segisaurus, and by Osborn[8] in Oviraptor; furthermore a specimen, probable referable to Velociraptor, recently collected by a joint Polish–Mongolian expedition to the Gobi Desert (Kielan-Jaworowska, personal communication) also appears to possess clavicles. Regardless of these few occurrences, however, the absence of clavicles in theropods is only negative evidence and, in view of the fact that the clavicle is dermal in origin, its absence in fossil specimens has no phyletic significance. It may well have been membranous (but not lost) in most theropods and thus not preservable.

The most likely origin of so many coelurosaurian features in Archaeopteryx is by direct inheritance from a small coelurosaurian ancestor. The additional significance of this phylogeny is that "dinosaurs" did not become extinct without descendants and I suggest that feathers, as thermal insulators, could be the primary reason for the success of dinosaurian descendants. Can it be just coincidental that mammals succeeded as therapsid descendants (at least partly) because of a comparable adaptation—perhaps acquired at about the same time?

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BOOK REVIEWS

Evolution of Geology

Charles Lyell: the Years to 1841: The Revolution in Geology. By L. G. Wilson. Pp. xiv + 553. (Yale University Press: New Haven and London, 1972.) £7.50.

CHARLES LYELL was one of the founders of modern geology and, in his time, one the greatest expositors of the subject. He, more than any other nineteenth century geologist, was responsible for removing the subject from the realm of speculation and conjecture, and establishing it on a sound philosophic basis. Lyell was also the friend, counsellor and confidant of Charles Darwin. Sir Archibald Geikie remarked many years ago that it is apt to be forgotten that Darwin started his scientific career as a geologist; and more recently the American author Loren Eiseley pointed out that the world tends to forget that Lyell wrote extensively on zoological subjects. The relations between Darwin and Lyell add materially to the interest of this new book.

Lyell's interest in geology was first aroused when, as an undergraduate at Oxford, he attended the lectures of William Buckland. After leaving Oxford in 1819 he studied and practised law for a few years, but finally gave up law to devote his life entirely to the advancement of geological science.

As an original observer, Lyell gained recognition quite early in his career; and the publication of his famous *Principles of Geology* (1830–33) greatly enhanced his reputation. In this work he defined geology as "the science that investigates the successive changes that have taken place in the organic and inorganic kingdoms of nature". The inclusion of organic nature in this definition is noteworthy. As a student of stratigraphy Lyell very soon became aware of the remarkable changes in animal life, exemplified by fossils, that marked the passage from past geological ages to the present day. Before Darwin came on the scene, Lyell had already given much thought to the problems raised by these changes.

The method Lyell used in carrying out his geological investigations is sum-marized in the sub-title of the *Principles* as "An attempt to explain the former changes in the Earth's surface by reference to causes now in operation". This method, later known as the principle of uniformitarianism (the name was coined by William Whewell), had been foreshadowed before 1800 by James Hutton (to whom Lyell made an acknowledgment), but in the *Principles* it was advocated much more clearly and convincingly, and was supported by a wealth of evidence that had not been available to Hutton. Gradually, though not without opposition, the principle of uniformitarianism came to be accepted by other geologists. It prepared the way for acceptance of Darwin's ideas about evolution, and before the end of the nineteenth century it had been adopted generally as the guiding principle for all geological research. Although Lyell advanced geological science in many other ways, this was his most important contribution to the subject.

Lyell realized the necessity for a geologist to widen his experience by travel, and he became an inveterate traveller, journeying to many parts of Europe and to North America. During these tours he consulted local geologists and exchanged information and ideas with them. Even during a honeymoon tour in Europe he took the opportunities offered to examine rock sections. Although he was a dedicated geologist, Lyell had other interests: history, politics, social problems and education, and for nearly fifty years he occupied a prominent position in both intellectual and social circles in Great Britain.

Hitherto the only detailed account of Lyell's life has been the two volume *Life, Letters and Journals of Sir Charles Lyell Bart.* (1891), edited by his sister-in-law Mrs [Katherine] Lyell. This is a mine of information, but there are gaps in the record, and the work makes no pretence to supply a critical account of Lyell's contributions to geology. Three short biographical accounts of Lyell's career have appeared since. T. G. Bonney's *Charles Lyell and*

Modern Geology (1895) was written by a geologist whose career overlapped that of Lyell, and it provides a nineteenth century assessment of Lyell's personality and his contributions to geology; E. B. Bailey's *Charles Lyell* (1962) is a much condensed version of Mrs Lyell's book, with added geological commentaries; while F. J. North's *Sir Charles Lyell: Interpreter of Modern Geology* (1965) is a brief account suitable for students and general readers. Lyell's importance as one of the leading scientists of the nineteenth century certainly justifies a new and more systematic account of his life and work; and Professor Leonard G. Wilson of the University of Minnesota is engaged in producing such a biography.

The author has been at work on this book for about ten years, and plans to complete it in three volumes. In preparation for the task, he first made an extensive search for new material, particularly for unpublished sources in archives in Great Britain, North America and elsewhere, and his search has justified the effort involved. The most important archive proved to be the mass of family papers preserved in Lyell's old family home in Scotland, Kinnordy House, Angus. Here, in addition to a very large number of family letters, often containing matter of geological as well as biographical interest, the author found Lyell's field notebooks and travel diaries, containing much information that had not been used by Mrs Lyell. The present representatives of the Lyell family generously allowed him complete freedom to examine and use for publication any material he thought suitable.

An important early find was the set of seven "Scientific Journals", in which Lyell recorded his private thoughts on the question of the transmutation of species, from 1858 to 1861, that is, the period immediately preceding and following publication of the *Origin of Species*. The length and importance of these journals justified separate treatment, and they have already been published[1]. A second important source

was the collection of letters received by Lyell, now in the library of the American Philosophical Society, Philadelphia. This archive contains 177 letters from Darwin to Lyell (most of which appear to have been published), and also 270 letters to Lyell from prominent geologists and other scientists. In passing, one cannot help expressing regret that the export of this great collection, sold at auction in 1950 for £5,200, was not prevented at the time, on the ground that it formed part of the British national heritage, an appellation which seems more appropriate for this collection than for some of the paintings about whose export there has been so much concern in recent years.

Professor Wilson has recorded his failure to trace all but a few of the large number of letters which Lyell must have written to Darwin, and concludes that they have not survived[2]. The explanation seems to lie in a statement made by Francis Darwin that, though Darwin's habit was to file letters, owing to his small stock of files, when these became full he burnt the letters of several years to free the files for further use; and this habit resulted in the destruction of nearly all letters received before 1862.

The first volume of Professor Wilson's work, which has the sub-title "The Years to 1841: the Revolution in Geology", takes Lyell's career up to that year. The author's term "revolution" clearly refers to the immense changes in geological thinking brought by the publication of the *Principles*. By 1841 geology was certainly on its way to becoming a science guided by reason rather than speculation, but it can hardly be claimed that the revolution was complete.

The author's treatment of his subject is chronological, but with the emphasis on Lyell's development as a geologist, the evidence that led him to formulate the principle of uniformitarianism, and his concern with the biological aspects of geology. An early chapter, entitled "The State of Geology in 1819", prepares the reader for what is to follow. Later chapters deal with more specific incidents in Lyell's career.

Thus, chapter 13 describes his relations with Darwin up to 1841. When, in October 1836, Darwin returned from the voyage of the Beagle, he was much concerned with the geological results obtained during the voyage. Lyell met him soon afterwards, and secured his election to the Geological Society on November 30, 1836. The two, having much of mutual interest to discuss, soon became close friends. Darwin's contacts with the palaeontologist Richard Owen are also discussed in this chapter.

Chapter 14 relates Lyell's involvement in the question of the age of the Crag (Tertiary) deposits in East Anglia. In assigning relative ages to particular beds he had reached his conclusions mainly by calculating the percentage of fossil shells present in each bed could be matched by forms still living in adjacent seas; and his conclusions had been criticized by local geologists. Lyell realized that the general application of this method required a skilled knowledge of conchology, and also general agreement as to what criteria should be used in defining species. Differences existed at that time between acknowledged experts in this field. It was typical of Lyell's thoroughness that in 1837 he made a prolonged visit to Copenhagen to study the species question under one of the experts, Dr Beck.

Chapter 15 discusses Lyell's reception of the new and revolutionary Glacial Theory announced by Louis Agassiz in 1840. Agassiz had demonstrated to Buckland evidence of the former presence of glaciers in Great Britain, and Lyell in turn was convinced after Buckland had shown him the field evidence. When, late in 1840, Buckland and Lyell jointly announced to the Geological Society their acceptance of Agassiz's Theory it created a sensation. Buckland informed Agassiz that Lyell had accepted his Theory "*in toto*", but, as Professor Wilson remarks, a long time passed before Lyell and his contemporaries accepted the wider implications of the glacial theory. The incident does, however, illustrate one aspect of Lyell's character, his willingness to accept from others new ideas, once convinced by the evidence.

As an example of how hard and conscientiously Lyell worked, it is worth mentioning that by 1840 the *Principles* had reached a sixth edition, each edition having been thoroughly revised; while in 1838 he had published a new work, his *Elements of Geology*, the first modern textbook for students of the subject. In a letter to his father, written in 1840, Lyell, referring to the publication of new editions, stated, "It is necessary to resist the temptation of coining money by simply compiling material provided by others instead of testing their accuracy by personally examining the facts in the field wherever they are easily come-at." Lyell was not an armchair geologist.

In July 1841, Lyell, accompanied by his wife, set out for America, where he remained a year. This journey was something of an adventure, and the present volume concludes with a letter to Lyell from his father urging him to take care of the health both of himself and his wife. Lyell was fortunate in having a father who encouraged his scientific aspirations and supported him financially when necessary (he eventually earned considerable sums from his books). His wife, too, shared with him the pleasures and hardships of many of his geological trips, on one occasion entertainment by the royal family in Denmark, but more often the discomforts commonly met with on geological field trips.

The first volume of this biography is a most interesting book, written in an unpretentious and readable style. It is illustrated with a number of contemporary portraits, and sketch maps of Lyell's tours; and it contains an extensive list of sources and an adequate index. In preparing it Professor Wilson has clearly been to great trouble to search out, collate and assimilate the large amount of source material available, much of it new. He makes no attempt to provide in this volume a detailed and critical assessment of Lyell's many contributions to geology, but he relates the part Lyell played in the gradual introduction of new ideas in the formative period of what was then the new science of geology, and his contacts with his geological contemporaries and other prominent scientists of the period. When completed this biography will provide valuable source and background material for students of the history of science in the nineteenth century, and it must certainly appeal to any geologist interested in the history of his subject.

V. A. EYLES

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The Story of Marconi

Marconi: a Biography. By W. P. Jolly. Pp. 292 + 24 photographs. (Constable: London, October 1972.) £3.95.

AN account of Marconi's early life inevitably reads like a compendium of biographical clichés. He was fourteen years old, and a scholastic failure, when Hertz discovered radio waves, yet he became the first person to harness them for communication. His father disapproved of his early experiments but his mother believed in him, and came with him to England when the authorities in his native Italy refused to sponsor him; within eighteen months he was back, a celebrity. He transmitted a radio signal across the Atlantic when established wisdom said it should have flown out into space, and he won a Nobel prize for physics after failing to gain entry to university.

Professor Jolly's impressively researched biography brings depth to this story without sacrificing readability, and his perceptive analysis makes Marconi's achievements credible without diminishing them. Radio in the 1890s, involving

a small number of imperfectly understood variables, is seen as being susceptible to empirical improvement by a resourceful and determined experimenter with no theoretical interest to distract or inhibit him. There are generous digressions to impart background information, and it is only very occasionally that these irritate by straying too far from the point.

Money was not of primary interest to Marconi, but the company that he founded to further the development of "wireless telegraphy" was often criticized for its aggressive business methods. Professor Jolly comments, with characteristic pithiness:

". . . the fact that the company was based on scientific innovation did not relieve it of the need to advertise, to impress investors, and to confuse competitors. Such ordinary commercial requirements precluded running the company as though it were some sort of sub-branch of a learned society, which was apparently what many critics of its methods wished."

Whatever the ethics of the Marconi Company, the author establishes from its archives, and from those of the Public Record Office, that both the Post Office and the Admiralty countered by engaging in decidedly sharp practice.

The success of the company was, of course, largely due to the work of its engineers, and readers familiar with the history of radio will be disappointed to find that such distinguished men as C. S. Franklin and H. J. Round receive little mention in this book; the reader may overcome this omission by referring to W. J. Baker's *A History of the Marconi Company* (1970), but it is nevertheless regrettable. Though technical matters tend to be played down, they are lucidly dealt with, thanks to the author's professional background in electronics. There are, however, two unfortunate slips: Hertz's transmitting apparatus is incorrectly described, whilst early long-range telegraphy is stated to have used wavelengths of "hundreds of metres", whereas in fact wavelengths of several thousand metres were always employed.

The book's longest chapter is devoted to the "Marconi scandal" of 1912–13. This concerned completely unfounded allegations that a Government contract had been corruptly awarded to the Marconi Company, and distorted allegations (though with some basis of fact) that ministers had used their privileged position to speculate profitably in Marconi shares.

Marconi himself was concerned only insofar as his name was inevitably besmirched, but the affair caused a great outcry and came close to wrecking Lloyd George's career. This complex story is skilfully summarized.

The years after 1918 saw one of Marconi's greatest triumphs—the development of the short-wave "beam" system—yet it was basically a period of decline. Many distinguished people paid social visits to Marconi's luxury yacht, which was also his floating laboratory. Lord Mountbatten, then a specialist in radio, was one of those able to ask his host specific questions, and is quoted as recollecting: "The impression I had was that at this stage, which I think was about 1926, he had lost close contact with all the developments, although they were being carried out under his aegis."

Marconi was a shy man, unexcitable in spite of his Irish/Italian parentage; in later life he became increasingly withdrawn, and no attempt is made to present him as a colourful personality. Neither is great emphasis given to the long, slow decay of his first marriage, or to his numerous love affairs, though they are treated with sensitivity and insight.

Professor Jolly has gathered much valuable material, particularly from the Marconi Company's own archives. Notwithstanding its considerable scholarship, the book is written in a straightforward, unforced style, and can thus be recommended to specialist and general reader alike.

KEITH GEDDES

How to Grow Crystals

Laboratory Manual on Crystal Growth. Edited by I. Tarjan and M. Matrai. Pp. 250. (Akademiai Kiado: Budapest, 1972.) £4.

THE modest title of this book indicates accurately its contents; it is a collection of recipes for experiments which either demonstrate various crystal growth phenomena or enable the reader to grow single crystals destined for applications based on their special properties. It is indeed an unusual book; I do not know another like it on this subject. It collects together the sort of notes that are usually compiled in individual laboratories and are duplicated for students' use. Here we have many recipes, by nineteen contributors, arranged so as to form a practical course in crystal growth. The need for such a book has often been mentioned at crystal growth conferences; the present volume aims to satisfy that need. Any individual laboratory may have its own programme of experiments covering a limited range of experience; here the experiences of many people, covering a wide range of phenomena and methods, are collected together for the convenience of teachers and students.

The first half of the book deals with basic phenomena, and gives detailed instructions for many experiments aimed at familiarizing the reader with the conditions for the spontaneous formation of crystal nuclei and the growth of various types of crystals: dendrites and whiskers as well as the usually more desirable polyhedra. Growth from solutions, melts and vapours, epitaxial growth of one species on another, the detection of dislocations by etching, and recrystallization in the solid state, are among the topics dealt with. The book does not try to deal seriously with attempts to understand the phenomena in terms of molecular processes, but each section starts with an introduction to give some sort of theoretical background for the experiments. Such introductory material is very necessary to provide a conceptual framework, and these paragraphs are for the most part soundly based; but some statements are questionable. For instance, the spreading of new layers from the corners of crystals growing rapidly in highly supersaturated solution is said to support Kossel's notion that layers start where energy release is greatest; actually Kossel only claimed the operation of this principle at very low supersaturation; at high supersaturations, convergent diffusion at the corners is sufficient explanation.

The phenomena dealt with in this section of the book are all concerned with the growth of individual crystals. The problems of bulk growth, which involve the number of spontaneously formed nuclei as well as their subsequent growth, are not considered at all. The influence of supersaturation and the presence of other substances might well form the subjects of instructive experiments which would make this course on crystal growth more comprehensive.

The second half of the book contains detailed instructions for growing large crystals by the various methods now in general use, from solutions, from melts by zone melting or pulling from the melt, and from vapours. The apparatus necessary is described in detail and the precise instructions on quantities and procedures are evidence that the information is based on first-hand experience. The book ends with some pages on the processing of crystals: cutting and drilling, grinding and polishing.

The advantages of bringing together contributions by many authors, each having first-hand experience in a particular field, are obvious. Such a book may lack consistency of style, and is frankly a string of recipes; but its value as a practical laboratory manual is great. It should be in the hands of all teachers and students of crystal growth, for it covers most of the practical aspects of the subject; the one

notable omission is a section of quantitative experiments on spontaneous nucleus formation.   C. W. BUNN

Physiology of Breathing

Comparative Physiology of Respiration. By John D. Jones. Pp. vi+202. (Edward Arnold: London, 1972.)   £4 cloth; £2 paper.

OF all branches of comparative physiology, respiration has a special appeal to biologists.   This is partly because of the great diversity of evolutionary adaptations, their range in vertebrates being wider in structure and function than those in, for example, the nervous or the cardiovascular system. Secondly, man may find himself in a variety of extreme conditions and environments in which it is the limitations of breathing which are the most obtrusive—in exercise, high altitude, diving, pollution and asphyxiation, and even in hot climates and outer space. This is presumably because the small size of our reserves of respiratory gases and the rapid effects of alterations in gas exchange cause more serious deterioration than does restriction of other bodily activities.   In these conditions we may envy our animal cousins with different adaptations, and try to emulate them by artificial means. The study of the comparative physiology of respiration has flourished in recent years. The research has direct relevance not only to man in unusual conditions, but also to respiratory illness where our adaptations cannot cope adequately with disease processes.

Dr Jones's book never fails to excite interest in the zoological adaptations of respiration.   It is avowedly teleological, and whether this is a fault or not can be argued.   Oddly enough, teleology can damp down speculation, for if every adaptation is appropriate there is no need to look for deficiencies and disadvantages.   Joseph Barcroft's attitude to teleology was complementary and may be preferable: that of noting the nature and degree of functional impairment that an evolutionary specialization may carry with it.   The book is also deliberately biased in favour of respiratory pigments and gas transport to the neglect of mechanisms of breathing and tissue respiration. Strictly speaking, the word respiration is more applicable to the latter two processes.

These approaches are legitimate author's privilege.   What is presumably not intended is the lack of up-to-date information on some topics. Acclimatization to high altitude has been profitably studied since 1964, the latest reference; foetal and neonatal respiration, surely an important aspect of comparative physiology, is almost ignored,

as are recent studies on the nervous control of breathing and the mechanics of the respiratory apparatus.   Some sections are inaccurate or confused; for example, the definitions of vascular resistance, the description of oxygen "buffering" by haemoglobin, and the role of peripheral chemoreceptors. There are errors in the references.

Some of these are small criticisms, and all may be corrected. The great merit of Dr Jones's book is that it arouses interest and provokes thought. Undergraduates, research workers and teachers will be stimulated and educated by it.   J. G. WIDDICOMBE

Semiconductors

Semiconductors and Semimetals. Edited by R. K. Willardson and Albert C. Beer. Volume 9.   *Modulation Techniques.* Pp. xiii+574.   (Academic: New York and London, June 1972.) $29.50.

IT is often said that research on conventional semiconductors such as Ge, Si or GaAs is nowadays merely a matter of dotting the i's and crossing the t's. Be that as it may, techniques are still emerging from work on these materials which are important in that they have wide applicability to the study of solids in general.   This book deals with an excellent example of such a technique, namely the use of modulation methods for observing weak structure in the optical spectra of solids. Although the high sensitivity of modulation methods has been known to physicists for a very long time, they have only recently applied them in this way. The motivation has been an improved knowledge and understanding of the energy band structure of solids beginning with semiconductors.

Study of the band edges either side of the fundamental energy gap of a semiconductor is eminently feasible by straightforward transmission measurements such as absorption, magnetoabsorption, cyclotron resonance or Faraday rotation. However, at energies appreciably removed from the energy gap, the transmission becomes too small and recourse must be made to reflexion experiments.   Unfortunately reflexion spectra are relatively diffuse, but the use of thermal, stress, electric or wavelength modulation lifts weak but sharp spectral features associated with critical points from the diffuse background. Assigning structure to particular critical points and hence determining their energies is assisted by the presence of symmetry breaking parameters either inherent in the modulation method or separately applied statically.

This ninth volume in the series *Semiconductors and Semimetals* will presumably find most usage as a source

of reference. It will be a welcome addition to the bookshelves of research workers in the field. Most of the chapters are written by authors who have established international reputations; they include B. O. Seraphin, R. L. Aggarwal and I. Balslev. The physical content is generally of a high standard but the editors have failed to eliminate a great deal of repetition amongst the authors.   Almost 1,000 references are included and a serious attempt has been made to bring the volume up to date by the inclusion of addenda added at the proof stage.   Even so, developments are only covered up to and including 1970 and, inevitably I suppose, the book is already two years behind "the state of the art". Minor criticisms include excessive verbosity' in the first chapter and a glib treatment of experimental aspects in places.

In conclusion, a major criticism of the series *Semiconductors and Semimetals* is the narrow coverage of material within the volumes published so far.   They are almost exclusively about III–V compounds.   Treatment of such topics as narrow band (hopping) and amorphous semiconductors is long overdue and semimetals should be given more emphasis to justify the series title.   A. K. WALTON

Muscle Regenerates

The Regeneration of Minced Muscles. By Brice M. Carlson. Pp. vii+128. (S. Karger: Basel, London and New York, 1972.) Sw. francs 49 ; £5.40 ; $13.75.

THIS book is volume four in the *Monographs in Developmental Biology* series published by S. Karger under the editorship of A. Wolsky. It is a short (128-page) lucid account of a field of work in which the author has already established himself as a leading authority.

As well as describing his own work Dr Carlson describes the earlier Russian work on which his own observations are based and also gracefully acknowledges the as yet unpublished work of some of his graduate students.

While the book is dominantly histological in character considerations of gross anatomy, biochemistry and functional characteristics of muscle regenerates are discussed. The author's style is clear and direct, and the standard of illustrations is high.

A final chapter, entitled "Epilogue", poses several interesting questions for future study, and discusses the potential use of minced muscle techniques in traumatic surgery.

Unfortunately this slim volume is priced at £5.40, but even so is likely to be the authoritative work on the subject for some years to come.

A. J. BULLER

Inflammatory Substances

Chemical Mediators of the Acute Inflammatory Reaction. By M. Rocha Silva and J. G. Leme. In collaboration with Hanna A. Rothschild. Pp. ix+263. (Pergamon: Oxford and New York, December 1972.) £6.

FELDBERG and his colleagues in the 1930s established histamine as a chemical mediator of inflammation. Since then, other possible components of the inflammatory response have been found, including 5-hydroxytryptamine, slow reacting substance in anaphylaxis (SRS-A), bradykinin, various chemotactic factors, rabbit aorta contracting substance (RCS) and prostaglandins of the E and F series. Each substance, as its involvement is proposed or demonstrated, has been regarded as the most important inflammatory mediator, only to be supplanted after a few years by the latest pharmacological fashion.

During the past few years we have passed from the bradykinin phase into the prostaglandin phase of inflammation, but this change of emphasis is not reflected in this book; perhaps partly because bradykinin was discovered and named by one of the authors, but mainly because there must have been an inordinate delay between writing the manuscript and eventual publication. This is sad, for in such a fast-moving field, as inflammation, it means the book is already out of date. For example, of more than 400 papers which the authors cite in the main chapter on chemical mediators, only forty-six were published in the last four years and sixteen of these came from their own laboratory. Thus, little cognizance is taken of work published since 1968 by Solomon and Juhlin, Kaley and Weiner, Crunkhorn and Willis, Spector and Willoughby, Greaves and his colleagues and Änggård and Jonsson, involving prostaglandins in the inflammatory response and that published in June 1971 from my laboratory, demonstrating that inhibition of prostaglandin biosynthesis may be the fundamental mechanism of action of aspirin and similar anti-inflammatory drugs.

The book consists of four chapters, each one of which is well written, fluent and lucid. The first deals with the history of the inflammatory reaction. The second describes methods of measurement of the inflammatory response and concentrates on techniques which quantitate vascular leakage by extravasation of dyes or carbon particles. It would have been useful if these methods could have been compared with the ones using extravasation of labelled large molecules as a quantitative method. Co-axial perfusion of tissue spaces as a means of collecting potential mediators of

inflammation is also given considerable space, but the important work of Lewis and his colleagues, who measure enzymes and other chemicals in the lymph draining an injured site, is not recounted.

The third and largest chapter concerns the chemical mediators and quite naturally devotes considerable space to arguing the case for the participation of bradykinin. The last chapter deals with the anti-inflammatory drugs and demonstrates well the difficulties encountered in proposing a mechanism of action for these substances before it was discovered that they prevented formation of prostaglandins.

The book, then, is a useful reference source for those interested in reading about the history of chemical mediation of inflammation up to 1968. Work published since then is not adequately reviewed.   J. R. VANE

Sound in Hologram

An Introduction to Acoustical Holography. By B. P. Hildebrand and B. B. Brenden. Pp. xii+224. (Adam Hilger: London, August, 1972.) £7.

THE purpose of this book, as stated in its preface, is an admirable one, namely, "To bring together the results of research in acoustical holography so that workers in non-destructive testing, medical imaging, underwater imaging, and seismic exploration can decide whether this new technique can be useful to them". The wave of interest which followed the publication in 1966 of the first papers on this subject brought with it not a few misunderstandings and fanciful claims concerning the results which were thought by some to be possible. An authoritative review of this kind is therefore to be welcomed. The text of the book is clear and concise, useful lists of references are included for further reading and there are more than eighty illustrations of actual holograms and reconstructed images, some of them published here for the first time, which have been obtained by the various methods described.

A short introductory chapter shows how the original Gabor concept of holography led to the Leith–Upatnieks system, in which the directions of the interfering beams are chosen to facilitate the suppression of the unwanted image. Chapter 2 gives the basic theoretical analysis of holography including the replacement of the reference beam by an electronic reference. Chapter 3 is devoted to a brief summary of the theory of the propagation of acoustic waves in liquids and solids, refraction, reflexion, radiation pressure and so on. There follows a detailed analysis of various ways in which a hologram can be built up by, for example, using a moving point

receiver to scan the field by measuring the phase and amplitude at each position and then using the signal to modulate a synchronously-scanned light source over a photographic film. The analysis includes the calculation of the angular resolution of scanned holograms and of the aberrations occurring at high scanning velocities. The use of time gating, as an additional means of rejecting unwanted data from particular regions of object space, is also mentioned. There is a chapter on the application of information theory to sampled holograms and results obtained with a circularly-scanned system are used to illustrate the conclusions reached. The theory of the interaction of sound and light at a liquid surface is described and applied to an important direct method of hologram formation. Other methods, such as the use of thermoplastic film as a detector and the optical heterodyne technique, are briefly described. Finally, some applications of acoustical holography are described. These range from well-established fields such as medical diagnostics and non-destructive testing to more tentative proposals relating to underwater acoustics and seismic exploration.   V. G. WELSBY

Crystal Spectra

Infrared and Raman Selection Rules for Molecular and Lattice Vibrations: The Correlation Method. By William G. Fateley, Francis R. Dollish, Neil T. McDevitt and Freeman F. Bentley. Pp. 222. (Wiley: New York and London, November 1972.) £5.45.

IN recent years there has been increasing interest in the analysis of the vibrational (infrared and Raman) spectra of crystals. This has been something of a "no man's land" between the normal territories of the spectroscopist and the crystallographer with, for the former, unusual notations and pitfalls to be overcome. Although the most direct approach to the analysis of crystal spectra—the correlation method—was developed more than twenty years ago by Hornig and Halford and their coworkers, the results of this method have not been systematically tabulated, with the result that a number of misunderstandings have led to mistakes in the literature. The aim of this short book is to present systematically the tabulated data and to apply these in detail to a sufficient number of examples to make clear the correct way of using the method and its scope. This is well and clearly done. The only criticism of the book is that it is very much a spectroscopist's publication dominated by the Schoenflies point group notation with which the reader is expected to be fully familiar. As crystallographers are

becoming increasingly interested in crystal dynamics it would have been advantageous to both sides if the relationship between the Schoenflies and Hermann–Mauguin symbolism had been made clear, the translation-containing symmetry elements of space groups described, and a discussion given of the derivation of the isomorphous point group from the symmetry elements of the crystallographic space group. However, this would have been mainly an educational gain, as for most particular examples the necessary relationships are to be found in the comprehensive tables.

The high price of this small book may be the result of the extended tabulated matter it contains. However, it is a very useful handbook which should certainly be on the bookshelves of all interested in the vibrational spectra of crystals, and a number of other spectroscopists besides.   N. SHEPPARD

Denaturation Dangers

Certainty and Uncertainty in Biochemical Techniques. By Harold Hillman. Pp. x+126. (Surrey University.: Henley-on-Thames, October 1972.) £2.85.

EVERY argument used in science has its loopholes, and some of the most dangerous are those easily forgotten because the arguments have ceased to be stated explicitly because they refer to popular techniques. Hence a book that aims to scrutinize the . assumptions of such techniques is welcome. In biology care must be taken to compare results at different levels of study, and the danger in the more controlled situations of the biochemist is that they are "unphysiological", frequently because the experimenter may alter his material in ways of which he is not aware. The author examines the .six techniques of subcellular fractionation, histochemistry, electron microscopy, measurements of radioactivity, electrophoresis and chromatography. After this he makes some general comments and summarizes his conclusions, largely that "an experiment is only as good as its controls".

Although several of the real difficulties of using and interpreting each selected technique are given, and several wise comments are spread throughout the book, its overall approach is largely spoilt by the author's concentration on heat. Because heating can harm biological material, each experimental situation is assessed largely in terms of the heating that occurs. Even that produced by impact of subcellular particles on the bottom of the centrifuge tube is

reckoned one of the dangers of subcellular fractionation.

Of course, the author is right that a protein may be denatured by heat during its extraction and that a procedure that keeps it cool diminishes this risk. But much can be done to assess whether the changes feared have occurred, by examining the homogeneity of the product and by comparing proteins extracted in different ways. This will not provide a complete answer, for a "denaturation" could involve the quantitative conversion of a protein into a single altered form. In the book such tests are little discussed and the reader is left with repeated warnings of the dangers of local heating and the difficulties of assessing its degree.

Electrophoresis seems to be a case where the author's concentration would be justified because most of the difficulty of scaling it up is the dissipation of heat. The rate of separation depends on the potential gradient, and the conductivity of the medium must be kept high because otherwise the substances being separated would significantly affect this conductivity. The potential gradient would then differ between the centre and edges of each band, and this would result in distortion and spread of each peak. But the author does not consider this, and discusses electrophoresis in terms of the differential heating of different bands. The controls of checking that the mobility remains constant, both with time and with potential gradient up to the highest used, are not discussed, let alone re-running of the fractions. I am not trying to deny the danger of overheating; indeed I have myself turned up the potential too high and seen a spot of haemoglobin that had been running nicely stop dead as it denatured. But here, as throughout, more emphasis on the possible checks, and less repetition of how unknown and dangerous heating effects are, would have given the book greater balance and value.   H. B. F. DIXON

Engineering in Context

Creativity and Innovation in Engineering. Edited by S. A. Gregory. Pp. 313. (Butterworth: London, 1972.) £5.

ANY word in the engineer's vocabulary that is associated with design seems doomed to ambiguity. For example, if you find the words creativity or innovation on the cover of a book you cannot tell what they are intended to mean until you look inside. Chameleon like, they take their colour from the leaves in which they are hidden. There is a whole spectrum of possibilities. At one extreme you find the enthusiastic

designer regarding creative work only meaningly portrayed in the work that has been created, that is, the final structure or machine. To him the elegance of the design and its embodied mathematics is the test of creativity. His book would be full of diagrams and calculations, for drawings would be his prose, mathematics his grammar, and differential equations his poetry. At the other extreme would be a book totally concerned with the context of designing, that is, the educational background, the commercial foreground and environmental constraints within which the designer must design. The spectrum ranges from pure content to pure context.

If you find it difficult to imagine a book on "creativity and innovation in engineering" which is totally concerned with .context and never shows or discusses a design at all, you can overcome your difficulty by buying one, for this is the title used by S. A. Gregory's book. It is a collection of papers prepared by the Design and Innovation Group of the University of Aston, Birmingham, under the joint sponsorship of the Working Party on Creativity of the Council Engineering Institution and of the Design Research Society.

Compressed into it are eighteen papers dealing with various aspects of the subject. Inevitably, perhaps, there is a good deal of overlap, but, surprisingly, there are noticeable gaps. For example, we are told on page 81 that "University education in Britain was until lately for the social elite and did not concern itself with the instruction and development of practical engineers at all". To many, like myself, who have been designing for many years by utilizing the realistic principles that we learnt in the Engineering Department at Cambridge, it is a little surprising to learn that, since 1783, the University has solely concentrated on training impractical engineers. Actually students at Cambridge have been required for many years not only to innovate new designs but each of them has his design costed, built and tested, and an account of this and the lectures on creativity would have added much needed substance to the section on education.

Although this book contains a useful summary of theories about the context of design, many of the chapters seem to finish before they have finished. Concluding is common, but conclusions are much rarer. Perhaps the best part of the book is the emphasis on the necessity of industry to exploit innovation and encourage an atmosphere that will breed it, but its general effect is·to give the impression that it is easier to break the subject up into little bits than to put it together again to present a unified and persuasive picture.

          G. L. GLEGG

CORRESPONDENCE

TAC

SIR,—I read with very great interest your article on the TAC Report (*Nature*, **241**, 2 ; 1973).

Our company, which through the Greenwich local television channel can claim, we believe, some responsibility for broadening the minds of the legislators, was similarly disappointed with the TAC Report. However, our trade association — the Cable Television Association—has already reacted by stating that it will shortly be producing its own plan for the future of broadcasting in this country. I am convinced that this will promote lively discussion about the great potential and versatility which cable offers.

Yours faithfully,

TIMOTHY DUDMAN

Albion Cablevision Limited,
58 Beauchamp Place,
London SW3 1NZ

Special Relativity Again

SIR,—Professor Ziman's admirable review[1] of Professor Dingle's book *Science at the Crossroads* covers most adequately "the question" raised by Dingle about special relativity, except for one point: Ziman invokes general relativity at a stage when it is not really needed.

In fact, while special relativity does not deal adequately with gravity, it does quite adequately cope with accelerated motion. In special relativity, just as in general relativity, the answer to Professor Dingle's "question" is: the fastest working clock between any two events is one that travels between them by free fall. Any other clock travelling between these events necessarily experiences inertial forces, which a physicist moving with the clock might interpret as being due to a (uniform) gravitational field; a physicist moving with the "fastest" clock would experience no such forces (he would be an "inertial observer").

This completely answers Professor Dingle's "question". It leaves unsettled the further question as to what it is that prescribes this particular structure for space-time. In special relativity, this structure is simply taken as given *a priori*; while this may not be thought to be a completely satisfactory answer (and general relativity gives a better

one), it is certainly at least a logically consistent answer.

Yours faithfully,

G. F. R. ELLIS

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and Theoretical Physics,
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[1] *Nature*, **241**, 143 (1973).

Reprint Requests

SIR,—The interesting article by Briggs and Briggs[1] on reprint request patterns under the deliberately misleading title "Hormones and Blood Chemistry" has moved me to make several comments about the reprint courtesy.

In 1970, some similar experiments on information retrieval techniques were conducted in *Nature*[2-4]. At that time, I had a pleasant exchange of correspondence with one of the principals (V. R. Pickles of Cardiff) through which we found ourselves to be in general agreement regarding uses and abuses of the reprint privilege. However, several mistaken impressions still appear to be fairly generally persistent.

There can be no argument that there is abuse of the reprint privilege by people who could determine whether or not they really need a reprint before they order it, by dabblers, and by habitual collectors ("scientific pack rats"). However, there is another side to the requesting of reprints through information gained from sources such as *Current Contents*. Many scientists work in places which are relatively remote from adequate library sources and they must gamble a bit on judgments about *Current Contents* titles to stay in the literature in their fields. If I might use myself as an example, I freely admit to errors in reprint ordering in the past and I acknowledge that I have some reprints which I can't use, but in most of these cases I was misled by titles. It would be impossible for me to check the actual contents of some journals without travelling literally hundreds of miles. I, and others in similar positions, must beg the indulgence of colleagues and we ask not to be lumped with the careless and abusive users of the reprint privilege. Of course, it could be argued that almost everyone should have access to *Nature*, but even this might not be the case.

I also sense that some of the concerns about reprint ordering by American scientists may arise from some mistaken impressions which are held by some workers in other countries concerning general working conditions in science in the United States. While a few workers here may have such financial and/or technical resources available that they can depend exclusively upon computer-based information retrieval done by hired assistants, most of us carry on the day-by-day slog through the literature which is the common burden of scientists everywhere. Hopefully, workable modern information retrieval will continue to become more readily available to everyone everywhere in the next few years.

Finally, one might ask how often these "experiments" need to be conducted in *Nature*. Publication costs and space limitations certainly would enter into such a determination. If further research is needed, possibly the editors could design even better "experiments" if they would construct an occasional *Nature* entry which incorporated into a single title such terms as "cancer, heart disease, racial differences in IQ, energy crisis, ecocide in Vietnam, and biological basis for female superiority".

Yours faithfully,

LELAND G. JOHNSON

Department of Biology,
Augustana College,
Sioux Falls, South Dakota 57102

[1] Briggs, M. H., and Briggs, M., *Nature*, **240**, 490 (1972).
[2] Davies, D., McKenzie, D. P., Turner, J. S., and Pickles, V. R., *Nature*, **225**, 636 (1970).
[3] Pickles, V. R., Davies, D., McKenzie, D. P., and Turner, J. S., *Nature*, **226**, 881 (1970).
[4] Pickles, V. R., *Nature*, **226**, 1181 (1970).

Nature's Parish

SIR,—At this juncture to ask the "academic community" to give Dr Kissinger "credit for his liberalizing influence in the past four years" is remarkable. As the use of violence during the Kissinger era has been liberal to the utmost extent, this statement (*Nature*, **241**, 1 ; 1973) ought, in fact, to be remembered and highly valued. The editor should be given credit for having given the ultimate expression to the complicity of the aca-

demic community in the crucifixion of Vietnam.

Yours faithfully,

KNUT ROGNES

Zoologisk Laboratorium,
Universitetet I Bergen

Who was HeLa?

SIR,—It is twenty-one years since George Gey established the famous HeLa cells in culture. It has been estimated that the weight of these cells in the world today exceeds that of the American negro from whose cervical tumour they originated. That lady has achieved true immortality, both in the test-tube and in the hearts and minds of scientists the world over, since the value of HeLa cells in research, diagnosis, etc., is inestimable. Yet we do not know her name! It has been widely stated that He and La are the first letters of her names but whereas one textbook says the names were Helen Lane another says Henrietta Lacks. My letters to the authors, inquiring the source of their information, like the letter to the hospital from which Gey's paper emanated, remain unanswered. Does anyone know for sure? Would it be contrary to medical ethics in the HeLa cell's coming-of-age year to authenticate the name and let He . . . La . . . enjoy the fame she so richly deserves?

Yours faithfully,

J. DOUGLAS

Department of Applied Biology,
Brunel University

Entropy and Vitalism

SIR,—Without even having read my book[1], Van Kley[2] refers to it as "a new form of vitalism" such that for evolution "different forms of the laws of thermodynamics apply". This is such a gross misinterpretation that I am compelled to object.

On page 22 I state: "I think our classical notions of entropy as they come to us from the presently established laws of physics and chemistry are totally inadequate in dealing with the living system. This does not mean that there is anything mysterious, supernatural, or vitalistic about the living system. It simply means that our classical notions are inadequate".

I should like to stress the word inadequate. For example, the laws of Newtonian mechanics are totally inadequate in explaining the shift in the perihelion of Mercury. Einstein's equations, which explained this quantitatively, are different in the sense that they are more general; Newton's equations are just a special case.

The concept of entropy in informa-

tion theory is far more general than in classical thermodynamics. Specifically, the entropy, H, as defined by Shannon[3], is

$$H = - K \sum_i p_i \log p_i \qquad (1)$$

where the p_i are probabilities of elementary events on a finite probability space and K is an arbitrary constant. If the p_i are all equal, then

$$H = -K \log p_i \qquad (2)$$

or

$$H = k \log W \qquad (3)$$

where W is the total number of elementary events on the space. But (3) is Boltzmann's definition of the thermodynamic entropy which appears as a special case under Shannon's more general definition.

Schrödinger[4] foresaw that we have given a positive name, entropy, to a negative concept—a measure of a kind of disorder. He proposed that we use the negative value of the entropy, the "negentropy", as a measure of the order or organization. I believe that Schrödinger was wrong. The true measure of the organization is the maximum value of the entropy, H^{Max}, minus the value we actually observe, H^{Obs}. H^{Obs} as a measure of the disorder has no structure, but $H^{Max} - H^{Obs}$ as a measure of the organization is rich in mathematical structure which classical theory neglected but which my theory stresses. It is in this sense a redefinition and extension of the entropy concept.

Consequently, I believe my work reduces the aura of vitalism man has always associated with the living system.

Finally, Van Kley certainly cited the wrong reference for any anti-evolutionary statement. Chapter 9 of my book is initiated by the following quotation from "The Giants" by Kahlil Gibran.

"I am among those who believe in the Law of Evolution; I believe that ideal entities evolve, like brute beings, and that religions and governments are raised to higher planes.

"The Law of Evolution has a severe and oppressive countenance and those of limited or fearful mind dread it; but its principles are just, and those who study them become enlightened."

Yours faithfully,

LILA L. GATLIN

Space Sciences Laboratory,
University of California, Berkeley

[1] Gatlin, L. L., *Information Theory and the Living System* (Columbia University Press, New York, 1972).
[2] Van Kley, H., *Nature*, **240**, 365 (1972).
[3] Shannon, C. E., *The Mathematical Theory of Communication* (University of Illinois Press, Urbana, 1949).
[4] Schrödinger, E., *What is Life?* (Cambridge University Press, London, 1944).

Synthetic Food

SIR,—The present is an especially opportune time for the initiation of a massive, interdisciplinary programme of research and development on the total synthesis of food.

Political as well as scientific leaders are coming to realize that agriculture, in the race with population, can at best only maintain the present 2,000-calorie-a-day diet in the developing countries. The "Green Revolution" and other recent advances are serving to gain time, but in a few years the population will outstrip the food supply *unless* the growth of population is quickly checked—an unlikely possibility—or unless an independent source of food is developed—a possibility that can be realized.

Two circumstances favour the immediate initiation of a major programme for the total synthesis of food. First, there is the availability of many scientists, engineers, and other experts who are now unemployed and would respond with alacrity to a new and challenging opportunity. Second, industry is at a stage at which it could adapt the vast fund of scientific knowledge and engineering experience amassed in the manufacture of synthetic polymers to the production of food.

Why has not a start been made? The answer lies in the problem of securing support for a programme of sufficient magnitude and duration to assure success. Experience in the administration of research has shown that support for a major, imaginative new programme can be obtained only after those proposing the programme have already made a significant beginning on their own resources. Research laboratories today that are competent to undertake a programme on the total synthesis of food already have a full complement of productive projects. Thus a new programme could be undertaken only at the sacrifice of currently successful activities.

The situation is similar to that which led to the beginning of the plantation rubber industry in 1876. Henry Wickham, later Sir Henry, discovered the unusually quick germinating characteristics of the seed of the *Hevea brasiliensis*. He chartered a steamer to bring seedlings growing in baskets of earth from the Amazon to London. Sir William Hooker, Director of Kew Gardens, threw out a collection of rare orchids to make space for the tender, little known seedlings until they should be ready to send to Ceylon, and later to Malaya. Since that time the billions of rubber trees on plantations have all been descendants of these original specimens.

Are there Britons today who have the

vision and the courage of Wickham and Hooker of a century ago?

Yours faithfully,

ARCHIBALD T. MCPHERSON

4005 *Cleveland Street,*
Kensington, Maryland 20795

Announcements

University News

Professor Paul Harrison Temple, University of Dar es Salaam, has been appointed to the Chair of Geography at the University of Birmingham, from June 1973.

Miss M. Hulme, Withington Girls' School, Manchester, has been appointed to the University Grants Committee.

Mr E. D. Mason, Director of Education, County Borough of Tees-side, has been appointed to the University Grants Committee.

Professor L. P. Harvey, Professor of Spanish at Queen Mary College, has been appointed to the Cervantes Chair of Spanish at King's College, London.

Miscellaneous

Professor R. T. Williams, St Mary's Hospital Medical School, has been awarded the CIBA Medal and Prize of the Biochemical Society for 1972.

Dr John M. Ashworth, University of Leicester, has been awarded the Colworth Medal of the Biochemical Society for 1972.

Professor D. J. Crisp, University College of North Wales, has been appointed to a visiting Professorship at the Federal University of Ceara at Fortaleza and will make subsidiary visits to Rio de Janeiro, São Paulo, Recife, and spend a short period in Argentina and Chile.

Dr R. Lee Clark, president of the University of Texas, M. D. Anderson Hospital and Tumor Institute, at Houston, has been chosen the recipient of the Sidney Farber Medical Research Award, previously given to Mary Lasker, Sir Alexander Haddow and Senator Lister Hill.

Dr Kent R. Van Horn, Vice-President of the Aluminium Company of America, has been awarded the Institute of Metals (Platinum) Medal.

Professor D. Hull, Department of Metallurgy and Materials Science at the University of Liverpool, has been awarded the Rosenhain Medal for his contribution in the field of physical metallurgy.

Erratum

IN the article "Normal Incidence Radiation Trends on Mauna Loa, Hawaii" by R. F. Pueschel *et al.* (*Nature*, **240**, 545; 1972) the second transmission equation in Table 1 should read $T = 0.9075 +$

$$0.000005175t - 0.00272 \sin \left(\frac{2\pi t}{365}\right)$$

$$+ 0.00164 \cos \left(\frac{2\pi t}{365}\right)$$

Addendum

IN the article "Mercury in Lake Sediments; a Possible Indicator of Technological Growth" by Aston *et al.* (*Nature*, **241**, 450; 1973), the term parts per billion (p.p.b.) was not defined. The usage throughout was American; 1 p.p.b. is equivalent to one part in 10^9.

International Meetings

March 12, Electron Sources for Microscopy and Related Techniques. (Meetings Officer, Institute of Physics, 47 Belgrave Square, London SW1.)

March 12–15, American Society for Neurochemistry. (Centre for Continuing Medical Education, The Ohio State University College of Medicine, 320 West Tenth Avenue, Columbus, Ohio 43210.)

March 12–16, Symposium on Nuclear Data in Science and Technology. (Dr L. Hjärne, Nuclear Data Section, Division of Research and Laboratories, International Atomic Energy Agency, PO Box 590, Vienna A-1011, Austria.)

March 14, Aspects of Process Development. (Assistant Secretary, Society of Chemical Industry, 14 Belgrave Square, London SW1.)

March 14–15, Sensory Appraisal of Difficult Foods. (Dr D. N. Rhodes, Meat Research Institute, Langford, Bristol.)

March 15, Spectroscopy and Anemometry by Photon Correlation Methods. (The Institute of Physics, 47 Belgrave Square, London SW1.)

March 19, Pesticides and the Processed Food Industries. (Conference Secretary, Society for Chemical Industry, 144 Belgrave Square, London SW1.)

March 20, Soil Responses to Long Periods Under Uniform Management. (Executive Secretary, 14 Belgrave Square, London SW1.)

March 25–30, International Symposium on Hepatotoxicity. ("KENES", Organizers of Congress and Special Events Ltd, PO Box 16271, Tel Aviv, Israel.)

March 26–27, Spring Conference for High Speed Photography. (C. W. Husbands, Central Unit for Scientific Photography, Royal Aircraft Establishment, Farnborough, Hampshire.)

March 26–28, Conserving Our Resources. (Conference Secretary, Society for Chemical Industry, 14 Belgrave Square, London SW1.)

Reports and Publications

not included in the Monthly Books Supplement

Great Britain and Ireland

Statistics of Smoking in the United Kingdom
·Edited by G. F. Todd. (Research Paper 1, 6th Edition.) Pp. 132. (London: Tobacco Research Council, 1972.) [3011

A Key to the Freshwater Fishes of the British Isles, with Notes on Their Distribution and Ecology By Dr. Peter S. Maitland. (Scientific Publication No. 27.) Pp. 139. (Far Sawrey, Ambleside: Freshwater Biological Association, 1972.) £1.20 [112

Wildfowl 23. Pp. 144+16 plates. (Slimbridge: The Wildfowl Trust, 1972.) £1.75; $5.50. [112

The Royal Society. Report of Council for the year ended August 31, 1972. Pp. 98. (London. The Royal Society, 1972.) [112

The British Council. Annual Report 1971 1972. Pp. 95. (London: The British Council, 1972.) [112

Estuarine Research: a Report on the Natural Environment Research Council Estuaries Forum held in the Summer of 1971. Pp. 20. (Publications, Series C, No. 8.) (London: Natural Environment Research Council, 1972.) [112

Bulletin of the British Museum (Natural History). Zoology, Vol. 24, No. 3: Miscellanea. Pp 157-228. (London: British Museum (Natural History), 1972.) £3.40. [412

Life with Diabetes. By Arnold Bloom. Pp. 30. (London: British Medical Association. 1972.) 13p. [412

University of Oxford. Annual Reports, 1970 1971. Pp. 27. (Oxford: The University, 1972.) 50p. [412

Proceedings of the University of Newcastle upon Tyne Philosophical Society, Vol. 2, No. 1: The German Linguistic Atlas. By A. W. Stanforth. Pp 1–14. (Newcastle upon Tyne: University of Newcastle upon Tyne Philosophical Society, 1972.) [512

Covent Garden Community Association. Report. Pp. 25. (London: Covent Garden Community Association, 1 Shelton Street, 1972.) [512

Technical and Specialised Periodicals Published in Britain: a Selected List. Pp. 264. (London. Central Office of Information, 1972.) [612

Some Fundamental Aspects of Urea Technology. By Dr S. M. Lemkowitz, Dr M. G. R. T. de Cooker, and Professor P. J. van den Berg. Pp. 102. (London: The Fertiliser Society, 1972.) [612

Philosophical Transactions of the Royal Society of London. B: Biological Sciences. Vol. 264, No. 864. The Growth of Children at Different Altitudes in Ethiopia. By E. J. Clegg, I. G. Pawson, E. H. Ashton and R. M. Flinn. Pp. 403–437. (London: The Royal Society, 1972.) 90p; $2.50. [612

Fifth Report of the Countryside Commission for the year ended 30 September, 1972. Pp. vii+52. (London: HMSO, 1972.) 57p net. [712

Department of the Environment. Getting the Best Roads for Our Money: The COBA Method of Appraisal. Pp. 17. (London: HMSO. 1972.) 32p net. [712

Loch Morar Survey. 1972 Report. Pp. 8. (London: Loch Morar Survey, 80 Palewell Park, SW14, 1972.) [712

A Little Book About Our Hearing. How We Measure Sound, How We Can Protect Ourselves Against Noise and What We Can Do To Make Noisy Machines Quieter. Pp. 14. (Hemel Hempstead, Herts: Atlas Copco, 1972.) [812

Education: A Framework for Expansion. (Cmnd. 5174.) Pp. iv+49. (London: HMSO, 1972.) 31½p. [812

PEP Broadsheet No. 539: Overseas Nurses in Britain: A PEP Survey for the United Kingdom Council for Overseas Student Affairs. By Michael Thomas and Jean Morton Williams. Pp. iii+54. (London: Political and Economic Planning. 1972.) £1. [812

Father of the Man. By Professor T. D. Foster. (Inaugural Lecture delivered in the University of Birmingham on 9 March, 1972.) Pp. 17 (Birmingham: The University, 1972.) 25p. [1212

Into Action: Plan for a Modern Employment Service. Pp. 27. (London: The Employment Service, Department of Employment, 1972.) [1212

Hillingdon Natural History Society. Bird Report, 1965–1970. Pp. 55. 50p. Mammal and Reptile Report, No. 1. By A. R. J. Paine. Pp. 9. 30p. Mammal and Reptile Report, No. 3. Edited by A. R. J. Paine. Pp. 16. 35p. (Uxbridge, Mddx.: Hillingdon Natural History Society, 4 Heron Close, 1970 and 1971.) [1212

Department of the Environment. Design Bulletin No. 26. New Housing and Road Traffic Noise—a Design Guide for Architects. Pp. 29. (London: HMSO, 1972.) 25p. [1312

Government and High Technology. By John Jewkes. (Third Wincott Memorial Lecture delivered at the London School of Economics and Political Science, 31 October, 1972.) Pp. 24. (London: The Institute of Economic Affairs, 1972. Published for the Wincott Foundation.) 50p. [1312

Patterns of Research. Pp. 44. (Newcastle-upon-Tyne: Procter and Gamble, Ltd., 1972.) [1312

Tin Chemicals for Industry. (TRI Publication No 447.) Pp. 32. (Perivale, Greenford, Middx : Tin Research Institute, Fraser Road, 1972.) [1412

Industrial Relations Training. Pp. 14. (London The Commission on Industrial Relations, 140 Gower Street, WC1, 1972.) *Gratis.* [1512

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Almost the Last Word on the Club of Rome

IT is now just over a year since Professor Dennis Meadows and his colleagues at the Massachusetts Institute of Technology published their tract *The Limits to Growth* under the auspices of the Club of Rome, and their argument has been a powerful stimulant of all kinds of public discussion. Because the complicated apparatus of mathematical equations which form the basis of Meadows's model has lent an air of mathematical precision to this work, the conclusions of *The Limits to Growth* have frequently been regarded as a proof of more qualitative gloomy predictions of what the future would be like. And because many politicians appear to welcome the great excitement about the natural environment there has been in recent years as an opportunity for effecting changes which might otherwise be politically impractical, *The Limits to Growth* has had an important influence on the attitudes of several governments—in Italy, for example, the general thesis that there are imminent dangers of collapse is understandably welcomed as a kind of explanation of the difficulties of regulating the economy of Italy.

Yet the tentative criticism which has been possible of *The Limits to Growth*, hampered as it has been by the lack of sufficient information about the assumptions on which the model has been based, has by now, in technical circles, led to the conclusion that the best thing to be said of the complicated model at MIT is that it is one of the most ambitious exercises in computer modelling so far undertaken which would have been of greater value if only greater care had been taken to make the assumptions explicit.

The irrelevance of *The Limits to Growth* to practical problems has now been finally underlined by the publication of a series of studies by the Science Policy Research Unit at the University of Sussex (*Futures*, 5, 1 ; 1973). The argument of Professor Christopher Freeman and his colleagues is all the more convincing because of its moderation. For example, Freeman says that he and his colleagues at Sussex are "in complete agreement" with the "MIT authors and their sponsors" about the urgency of many of the social problems with which *The Limits to Growth* is concerned. He also says that there is no quarrel about the desirability of mathematical models in the social sciences. Freeman is even generous saying that the construction of Meadows's computer model is "courageous and pioneering"—others may fairly say that it is brash and even foolhardy. The nub of the criticism from Sussex is that the assumptions used in constructing the Meadows model do not correspond accurately enough to the real world for the computer projections to be regarded as reliable guides to action in future. The Sussex team goes on to make the sensitive point that in circumstances in which the overriding need is to use the techniques of computer modelling as a method of understanding the relationship between different sociological variables, itself a formidable task, there is bound to be an element of subjectivity in ambitious schemes of computer modelling, and that it might be better to acknowledge that exercises like that of Meadows and his colleagues should openly be regarded as components of a political debate.

The Sussex criticism is based on the published volume *The Limits to Growth* and on an early draft of the technical report which was originally said to be due for publication in 1972. By all accounts, publication of this crucial document, in its final form, will now be delayed at least until the summer of this year. The Sussex criticism is accompanied by a rebuttal from Professor Meadows and his colleagues which raises important issues about the professional ethics of scientific discussion in this field. Thus Meadows says "inexplicably, the Sussex group has chosen to release its criticism before the last technical document becomes available to the scientific community" and elsewhere says, in a footnote, that advance copies of the technical report are available in photocopied form already. What Meadows implies is that scientific criticism of *The Limits to Growth* should have been held over until the much postponed technical description of the assumptions on which the computer model is based had been completed. What he overlooks is that one of the most damaging criticisms of his exercise in computer modelling is that *The Limits to Growth* itself should not have been published without a full description of its assumptions. Undergraduates instructed in the techniques of computer modelling are—or should be—told quite firmly that a model is of no value to others unless its assumptions are made explicit and are open to technical discussion. What Meadows seems to be asking for is the best of both worlds —he wants *The Limits to Growth*, with its stark and astonishing projections of the future, to inform the political decisions of governments but that technical criticism from his professional colleagues should be held up until he gives the signal. The truth is, however, that *The Limits to Growth* itself contains enough errors and inconsistencies to sustain the kinds of criticism which the Sussex group and others have advanced. If it should be that the final version of the accompanying technical report turns out to make the absurdities of *The Limits to Growth* less obvious, it will be an important public question to know whether that document should be regarded as the guide to action which the Club of Rome hoped it would be. It should perhaps be added that advance copies of the technical report are not nearly as freely available as Meadows says—he has, for example, declined to supply one to *Nature* on the grounds that "you will only use it against us". It is hoped that the muddle—to say the best of it -- created by this slapdash method of publishing a scientific thesis will be a warning to others who may follow with computer projections of the future.

In detail, the criticisms which the Sussex group has to make echo the previous criticisms which have been made of *The Limits to Growth*. First of all, the group emphasizes that the validity of any computer calculation depends entirely on the quality of the data and the assumptions which are fed into it, and warns against the dangers

of "computer fetichism". Somewhat generously, the Sussex group defends Meadows against the implications of the charge "garbage in, garbage out", but goes on to assert that although the Meadows model is not strictly Malthusian, it is fair to level at the MIT work the jibe "Malthus in, Malthus out". What this implies is that the parts of the MIT model dealing with population make no allowance for the way in which population growth is determined—as the demographic history of the past century shows clearly enough—by changes in family habits just as much as by physical considerations. The Sussex group also points to the now well-known weaknesses of The Limits to Growth model and its assumptions of how mortality, for example, is related to worldwide levels of pollution, an issue on which there is no scientific evidence on which to base assumptions of any kind. The criticism continues with an account of how the assumptions in the model of the likely exhaustion of natural resources are over-simple and over-rigid. The plain truth is that anyone who assumes that there is a literally finite supply of natural resources—250 years supply of everything at the present rate of consumption in the original Meadows model—and who neglects such things as the influence of the price mechanism on the rate of consumption and the likelihood that new discoveries will be made in the future as in the past will inevitably conclude that there must at some stage in the future be a catastrophic collapse of the industrial economy. Yet in the long run, the most likely happening is that industry will be compelled by the increasing scarcity of some of the materials now inherently a part of industrial life to switch to others which are intrinsically much more plentiful. This is a splendid example of how the supposedly objective Meadows model turns out to contain a built-in bias in favour of collapse in the not too distant future.

The Sussex group rehearses other now familiar difficulties with the Meadows model, but does so moderately and with the advantage of knowing what the early draft of the famous technical report contains. There are arithmetical inconsistencies as well as economic anachronisms built into the parts of the calculation dealing with capital investment. The relationship between industrial activity and the generation of pollution assumed in the model is over-simple and misleading. The computer loops dealing with agricultural productivity make too little allowance for beneficial change. In all the circumstances, it would have been more prudent if Meadows, in his reply, had been more willing to acknowledge the cogency of these criticisms. Instead, he blusters, complaining that "the Sussex authors have not put forward an alternate (sic) theory of growth to support their views", as if it were incumbent on critics always to follow the precedents of those they criticize. He goes on to complain, unfairly, that the work of the Sussex group implies that "present short-term reductionalist predictive models are appropriate for addressing the causes and consequences of population and material growth"—the point is that the papers from Sussex acknowledge that the problems which worry Professor Meadows and other people are legitimate concerns but raise the question whether they can properly be handled by computer models in the present state of uncertainty. Meadows seeks to distinguish between "the numerical properties of our preliminary world models" and the "basic dynamic attributes" of the world system described in The Limits to Growth, arguing that exponen-

tial growth in a physically limited world leads to inherent instability, and that this aspect of the problem demands urgent study "whether or not the precise assumptions of our particular computer model are ultimately accepted". In reality, however, what the Sussex group, like previous critics, has done is to point out that the mechanisms of exponential growth and the assumptions of rigid physical limits which characterize The Limits to Growth are themselves untenable: the argument is only partly about numbers and is more cogently concerned with the character of the assumptions made. Against this background it is hard, with the best will in the world, to accept seriously Meadows's own list of "the errors" which the Sussex group has allegedly made. Indeed, some of the details of the Sussex work which Meadows describes as erroneous deserve some quite different description altogether. It is, for example, absurd of him to complain that it is an error for the Sussex group to argue that not enough is at present known of the ultimate availability of natural resources and then to go on to say that the estimates in The Limits to Growth are too conservative. Is Meadows really wishing to imply that in circumstances in which certainty is unattainable, it is legitimate for those who build computer models to make whatever assumptions they choose, even when these are known to be too limited?

The essence of the Sussex criticism is that the Meadows model is too inaccurate a representation of the real world to be a reliable projection of the future, but the issue of principle which divides the two groups is their attitude towards technical progress. It has been said, of The Limits to Growth, that many of the gloomy projections stem directly from the assumption that present gloomy trends—the pace of population growth, for example—will continue as they are until checked by physical shortages, but that recent optimistic trends, such as the steady improvement of agricultural productivity and the development of new techniques for the exploration for and the exploitation of new mineral resources, will come to a halt. It is true that nobody can predict just what technical skills will be accessible to the human race decades from now, but surely it is quite absurd, after the experience of the past century, to suggest that there will be no improvement of the techniques by which people at present survive on the surface of the Earth. To say this is in no sense to imply that scientific research and technical development contain in themselves the secret of survival, but there is the strongest possible reason for expecting that technology will continue in some shape or form. Indeed one of the morals that might have been drawn from The Limits to Growth is that there is an urgent need for scientific research and technical development in some of the areas such as energy supply in which Meadows and his colleagues do not have a monopoly of concern. It is fashionable among some environmentalists to complain of those who would allow for the likelihood that survival skills will continue to become more sophisticated as "technological optimists". What that canard implicitly denies is that the survival of the human race so far, in the past five hundred thousand years or more, has depended on a continual enhancement of skill and that, even if it were now possible to halt some of the tendencies such as population growth which cause anxiety, survival would require a continuing search for better techniques. Computer modelling itself is such a skill. What this argument has shown is that there is still a long way to go.

Five Years More

THE British government is wise to have acknowledged that it cannot hope to work out a long-term strategy for broadcasting in Britain by the time the franchise of the BBC and the constitution of the Independent Broadcasting Authority are due to be revised in 1976, but it is less certain whether a postponement of the decision until 1981 is strictly necessary. Everybody will agree that it would be wrong to rush a decision on long-term strategy without first carrying out the technical studies and the consultations on which a sound policy might be based, but a postponement of five years is almost the same as a decision not to think about the broader issues in the lifetime of the present Parliament or even, possibly, during that of the next. To be sure, the government has said that it will push ahead with a decision about a fourth television channel and that it feels free to think again about the method of financing the BBC's operations, at present dependent on licence fees collected from the public. But there is the strongest possible case for asking that a quick start should be made on several issues likely to determine the pattern of broadcasting in the 1980s.

One important issue, for example, is the extent to which the BBC should continue in its present form as an autonomous organization responsible both for the production of programmes and for the transmission of electromagnetic waves. The corporation's competence and reputation in both fields is outstanding but it would be an economy and probably a qualitative benefit as well if the engineering side of the corporation's function were amalgamated with that of the Independent Broadcasting Authority. It is, of course, essential that in any reorganization of the BBC, the editorial independence of the programme-making function should be guaranteed and it is even proper to ask whether this might not in future be more safely assured if the corporation's trustees, the Board of Governors, were provided with an annual grant and not the necessarily uncertain and static revenue from licence fees.

A second group of questions is technical. Largely because Britain is geographically crowded, the number of television channels available at the UHF band is limited, with the result that British television is unlikely ever to consist of more than four channels so long as old-fashioned broadcasting is the principal method of transmitting signals. This is why it is inevitable that there should be a rapid growth of cable television in the decades ahead. One of the questions to be decided is who should own and operate a cable television network, and how arrangements should be made for supplying it with programmes. Technically, there is the strongest possible case for an integrated network of cables through which a variety of programmes could be supplied. The ideal, no doubt, is that the network should be publicly owned and that it should be possible for its operators to make charges on those who use it in much the same way as telephone subscribers now pay different charges for different kinds of telephone calls. But the government should not let its hankering after control delay the introduction of an essential service like this when commercial companies are only too ready to provide the capital. The first need, in any case, is for a further technical examination of the problem but the second is for an examination of the problems in providing a cable television network of programmes—one of the virtues of the system is that it should make possible local community broadcasting, another is that it should allow people to have television programmes from other countries, no doubt at a different price. It will be a scandal if this is much delayed.

100 Years Ago

THE CHALLENGER EXPEDITION

H.M.S. *Challenger* cast off from the jetty at Portsmouth at 11.30 A.M. on December 21, with a low barometer. A strong south-westerly breeze was blowing, and the drum up; so that, especially in a season like the present, the prospect was not promising for the first few weeks of her voyage round the world.

The result justified the drum, and for a week we were knocking about the mouth of the Channel, and the Bay of Biscay, making slow progress southwards. It was perhaps as well to get a good shaking at first. It showed at once where there was a screw loose, and gave a chance to tighten it up. A sharp cyclone which caught the ship on her way from Sheerness to Portsmouth had already tested pretty fully the stowing of the apparatus, and although the *Challenger* rolls considerably when she is put to it (over 35°), not a single instrument shifted, and not a glass was broken, either in the zoological workroom, or in the chemical laboratory. Just before we got to Lisbon the weather improved a little, and we got some soundings and took one or two trial hauls with the dredge.

After leaving Lisbon on January 12 the wind was again fresh, but between Lisbon and Gibraltar we made some important experiments, and found, among other things, that we could work easily and successfully with the common trawl down to 600 fathoms. I am now writing about 100 miles north of Madeira, and since leaving Gibraltar the weather, though at first breezy, has been on the whole fine. We have taken several successful navigative sounds at great depths, and we have trawled successfully at 2,125 fathoms, and recovered many interesting animal forms, several of them new to science, and others of extreme rarity and beauty. Still we must regard our work up to the present time as only tentative. The weather has been against us. It is altogether a new experiment to dredge from so large a ship, and it seems to present some special difficulties, or at all events to require some management. The weight of the ship is so great that there can be no "give and take" between it and the dredge, such as we have in the case of a smaller vessel. If there is any way on, the impulse to the dredge is irresistible, and seems to tend to jerk it off the ground. This difficulty can no doubt be met, but the only way of meeting it appears to be by using a length of rope greatly in excess of the depth—and having weights. A single dredging operation may thus occupy a great length of time, but in compensation we have the greater size and efficiency of this dredge. The few trials which we have already made have been all in the direction of improvement, and I have little doubt that under Captain Nares' skilful management what little difficulty is still felt will shortly disappear. ● ● ● ●

WYVILLE THOMSON

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OLD WORLD

Launchers for Europe?

THE question of whether United States rockets will be used to launch European communications satellites was carried right into the American camp last week. Professor Maurice Levy, chairman of the council of the European Space Research Organization, took the opportunity of an address to the American Astronautical Society in Washington to demand a guarantee from the Americans that their launchers will be available for European communications satellites as well as for scientific and other applications satellites. Otherwise, he said, Europe will have to envisage continuing her own launching activities.

The United States has already given general assurances that any country's scientific and applications satellites will be launched provided that they are for peaceful purposes and that the obligations of the United States under international arrangements and agreements, such as Intelsat, are honoured. But the offer of launchers for communication satellites is hedged about with conditions that make it anything but an open assurance.

So far, all Europe's scientific satellites have been launched by the United States. But, when Europe's first communications satellite becomes due for launch in 1979 or 1980, commercial considerations will come to the fore for the first time. What Europe wants is a plain statement from the United States that all its satellites will be launched, regardless of commercial interests.

"The Europeans," Professor Levy said, "will endeavour to avoid duplication and waste in the space field. . . . If Europe can obtain a real guarantee that American launchers will be supplied for all European satellites developed for peaceful purposes, then the community of European countries may consider giving up their own launcher programmes. . . . Only real guarantees on the granting of licences for the construction of launchers, and more generally on the availability of American launchers, could lead Europe to reconsider her position".

The problem, for ESRO, is one of some urgency. Three applications satellites were approved by the organization's council in 1971, and the launch date for the first of these is only three years away. The chances of the European Launcher Development Organization having the French-designed L3S ready for operation by then must, on past showings, be remote. The rocket is still largely on the drawing board even though it uses some existing com-

ponents, and ELDO is about to go through a time-consuming reorganization as it becomes part of the proposed European Space Agency which is to come into existence on January 1 next year.

With two of ESRO's three applications satellites there should be no problem. AEROSAT, part of an international air traffic control programme, is in any case a shared programme with the Americans, so a launcher for that in 1976 is no problem. Similarly ESRO's meteorological satellite, part of the World Weather Watch programme and also due for launch in 1976, presents no commercial threat to the United States.

But ESRO's European Communications Satellite (ECS), a test version of which is to be flown in 1976 and full versions of which are planned for 1979 or 1980, is another matter. Designed for intra-European communication the satellite will handle telephone, telegram, telex and television channels and must be considered viable.

Professor Levy emphasised in his speech recently that one of the most important objectives of Europe's space programme for the 1980s is to meet user requirements. This involved, he predicted, not only communications satellites but also relay satellites served by numerous small terminals designed to meet the specific requirements of users such as newspapers and banks.

But before ESRO has to have launchers for its communications satellites, the French and Germans need one to launch their communication systems Symphonie I and II. At present these are to be launched on Europa II, but the programme may well be scrapped before their launch date (see Nature, 241, 359; 1973), in which case an American (or Russian) launcher will be the only way to fly the satellite, and the indications are that the Americans will launch it.

CONTRACT RESEARCH

Fulmer-Yarsley Merger

THE Fulmer Research Institute, owned by the Institute of Physics, is to merge with Yarsley Research Laboratories (YRL) to form a company with a turnover of £750,000 a year. Fulmer confidently expects this figure to rise to £1 million a year in 1975.

Fulmer and Yarsley are no strangers to each other, for each company has in the past done sub-contracting work for the other. But after May 1, 1973, the links will be much closer and will allow the new company to offer customers a wide range of expertise. In the past, Fulmer has been noted for its work on surface coating and alloy development among other things whereas YRL has been strong on polymers and plastics.

YRL at present operates at Chessington, Surrey, where there is little room for expansion and, through its subsidiary Yarsley Technical Services (YTL) at Ashstead, Surrey. The plan is that the activities at Ashstead will continue as before, although the shares in YTL will be held by Fulmer, but that work at Chessington will be transferred to the new Yarsley laboratories at the Fulmer site in Stoke Poges by the end of September.

The new combined concern will employ 200 staff of whom 85 are professionally qualified. In 1971 Fulmer had a turnover of £467,000 and made a profit of £15,000 after paying £12,500 to

Turnover of British Independent Contract Research Organizations (1970)

	£ thousand
Huntingdon Research Centre	2,000
International Research and Development	1,100
Robertson Research International	740
Ricardo and Co.	740
Fulmer + Yarsley	590
Inveresk Research International	250

the Institute of Physics. The profit for 1970 was much higher—£25,500—but in that year the Institute of Physics received only £9,100 (see Nature, 232, 4; 1971). Also Fulmer spent £12,000, a particularly large amount, on taking out patents in 1971. YRL, on the other hand, had a turnover of £220,000 in 1971-2 and made a modest profit of £4,000.

How will the new Fulmer Research Institute compare with other contract research organizations in Britain? The Table shows the situation in 1970. Evidently Fulmer will be within striking distance of the four largest companies when the merger is complete. Overall, contract research in Britain is now worth about £12 million a year, which includes more than £3 million from contract research activities at Harwell. This is still much less than the amount spent in the United States on contract research; there the total market is more than £250 million a year and the largest companies, the Battelle Institute and Stanford Research, each have an annual turnover of about £50 million.

URANIUM ENRICHMENT

European Plant Planned

PRESSURE is growing for a European uranium enrichment plant. A report by the Parliamentary Committee on Energy, Research and Atomic Problems, which is to be presented to the European Parliament on Saturday this week, urges the community to establish a joint undertaking to study the problem of uranium enrichment in order to provide, by June 30, 1974, for a decision to be taken on which system should be built commercially.

The committee's report backs up almost to the last detail the recommendations that the European Commission has been making for some time. Two years ago the commission pointed out that by 1980 there would be a marked shortage of uranium enrichment capacity in the world. By 1980 Western Europe will be generating 70,000 MW of electricity by nuclear power; by 1985 output will have risen to 160,000 MW, according to the commission.

Enriched uranium is currently supplied by the United States Atomic Energy Commission, but its capacity will be only 26 million separative work units by 1980, and Europe's requirements alone will be 10 million SWUs in 1980 rising to 19 million units by 1985. As a result, the commission concludes that nuclear power stations ordered after 1974 cannot be sure of supplies of enriched uranium unless Europe builds its own plant.

The commission sent a draft resolution to the council of ministers last year urging it to establish a joint undertaking to study the problem. It is this recommendation that the parliamentary committee has now backed.

But the parliamentary committee emphasizes in its report that unless a political decision on a community energy policy is taken, no decision on a uranium enrichment plant can be made. Ministers are meeting to discuss, and hopefully devise, a common energy policy in May.

The committee's other chief recommendation is that, at first sight, there is no reason why more than one uranium enrichment method should not be developed by the community. Part of the problem is that there are three methods available; the question is which to choose.

Gaseous diffusion is the traditional method and is used in the United States. Nozzle separation, which is being studied in West Germany, is still in its infancy and is unlikely to be in the running for some years yet unless an enormous amount of effort is put into it. The gas centrifuge is the real alternative to gaseous diffusion. Britain has worked on the gas centrifuge for

some years now and in 1971 a joint company was formed between Britain, Holland and West Germany to study ultracentrifuge separation.

Its protagonists claim that the centrifuge will ultimately prove far more economic than gaseous diffusion. Dr Jack Parry, technical director of URENCO, the marketing part of the tripartite centrifuge project, told a conference in Tokyo last week that from an investment point of view the centrifuge now looks viable. Backers need to be sure that the capital cost of plant can be predicted accurately before they agree to invest in it. "We have no hesitation in believing this to be the case," Dr Parry said.

An additional spur to the European programme is the proposal by the United States to raise its prices for enriched uranium by more than a third. Such an increase could go some way to making the centrifuge more economic more quickly.

SCIENTIFIC JOURNALS

ZhETF Centenary

from our Soviet Correspondent

THE Russian *Journal of Experimental and Theoretical Physics* (*Zhurnal Eksperimental'noi i Teoreticheskoi Fiziki—ZhETF*) is this year celebrating the centenary of its publication. This journal, the oldest Russian periodical devoted to the physical sciences, started life as the official organ of the Russian Physical Society which was founded in March 1872. The first issue of the journal appeared early the following year.

In 1878, the Russian Physical Society amalgamated with the Chemical Society, and the joint publication of the combined body became the *Journal of the Russian Physico-Chemical Society* (*Zhurnal Russkogo Fiziko-Khimicheskogo obshchestva — ZhRFKhO*). The physics section of this journal, however, retained its separate pagination and its own editor and was virtually still an independent journal. In 1907 it once again resumed separate publication.

During its existence as the physics section of *ZhRFKhO*, its contributors included such eminent names as D. I. Mendeleev, P. S. Erenfest, V. K. Lebedinskii, and A. F. Ioffe. Up to 1917 its size remained small, averaging only thirty printed pages a volume.

The *ZhRFKhO* survived under its old title until 1930, when, as part of a general reorganization of scientific societies and institutes, it was transformed into its present form as the *Zhurnal Eksperimental'noi i Teoreticheskoi Fiziki*. Since then its editors have been A. I. Ioffe and L. I. Mendel'shtam (1931–39), S. I. Vavilov (1939–52), N. N. Andreev (1952–56) and P. L. Kapitsa (1956–).

ENVIRONMENT

Whiskey in the Jar

THERE is little fear that man will exhaust the mineral resources of the Earth, according to Professor D. D. Hawkes of the University of Aston. Delivering his inaugural lecture as professor of geological sciences, Dr Hawkes maintained not only that the 17 million million million tons of material in the outer ten miles of the Earth's crust contain enough metal to meet all man's needs provided he can extract it, but also that ores are still being formed.

Manganese nodules may be accumulating some minerals faster than man currently uses them, hot brines containing abnormal quantities of Mn, Zn, Cu, Pb, and Ag are forming beneath the Red Sea, and volcanoes can and do produce economic deposits—for example the 160 million tons of ore deposit (with an average content of 35 per cent) found in the Matsuo crater.

Professor Hawkes also took issue with estimates of current reserves. Based as they are on the limited data available which list only known deposits of ore and which assume no progress in mining or prospectiing technology, they are "always unreliable and invariably on the pessimistic side".

The ocean floor may well contain large quantities of ore, and a "great untapped mineral potential" lies beneath the continental crust. This crust is more than 25 miles thick in places but radically new methods of mining could enable man to conquer the "depth barrier".

Professor Hawkes went on to urge that a wide-ranging survey of Britain's mineral deposits should be launched, complete with exploratory drillings. Further, parliament should pass an act declaring all minerals the property of the state, for private ownership of mineral rights in Britain causes serious delays in the development of Britain's mineral resources.

Professor Hawkes also defended the findings of Lord Zuckerman's commission on mining and the environment which was sponsored by Rio Tinto Zinc and six other large mining companies.

Mineral prospecting in National Parks also received Professor Hawkes's approbation. Prospecting and exploratory drilling, he argued, causes little damage to the environment. After full-scale mining "the environment—admittedly in a changed form—is still there", and the change need not be a great one. A different emphasis in our attitude to the environment is needed, Professor Hawkes said. "If a copper deposit is discovered in North Wales, should we not be saying—'how can we mine it with least interference to the environment?'. Not, as at present, 'North Wales is beautiful; we cannot have a mine there'."

Human Experimentation and Medical Ethics

by our Washington Correspondent

FOR the past 40 years, a number of poor uneducated black men in Alabama have been taking part in a medical experiment without their knowledge or consent. They were all found to have syphilis in 1932, but treatment has been withheld from them—even after penicillin became available—because the investigators wanted to determine the clinical effects of untreated syphilis. The experiment, known as the Tuskegee Study after the Alabama town in which it took place, was brought to light last year by a reporter working for the Associated Press, and it has become perhaps the most visible scandal involving medical research in the United States.

When the Tuskegee study first hit the headlines, government officials pointed out that although the study was carried out by the Public Health Service, they were unaware of it. They promised to provide free health care to the survivors (a promise which has yet to be kept) and pointed out that the study was initiated 40 years ago, when medical practice and social conditions were very different—guidelines and controls on medical research are now sufficient to prevent such abuses taking place, it was suggested. But several witnesses who testified before the Senate Health subcommittee during hearings on human experimentation last week were much less sanguine.

The hearings brought to light a number of abuses of medical practice which Senator Edward Kennedy, the chairman of the subcommittee, described as "outrageous". The committee was told, for example, of a study carried out last year in San Antonio, Texas, in which a number of Mexican-American women who went to a family-planning clinic were given placebos instead of oral contraceptives as part of a study to determine whether the side effects of the pill are physiological or psychological. Although told to continue practising whatever form of birth control they usually used, at least ten of the women quickly became pregnant.

In another case, an experimental method of inducing abortion was carried out on 15 women in Philadelphia in May last year, as a result of which one eighteen-year-old woman had to have a complete hysterectomy and eight others had complications. According to Dr Sidney Wolfe, a doctor associated with an organization called the Health Research Group which is linked with Ralph Nader, the method, known as the supercoil, had previously been condemned as

scientifically unsound and the women on whom it was used were not adequately informed of the risks involved. In a previous set of hearings, (see *Nature*, **242**, 7 ; 1973), Kennedy's subcommittee had also brought to light incidences of routine prescribing of drugs for uses not approved by the Food and Drug Administration.

Fortunately, such cases of seemingly obvious abuse of medical ethics in research involving human subjects are rare, but several witnesses suggested last week that they simply represent the tip of an iceberg of questionable research practices and studies which have dubious scientific merit. Such a situation led many to recommend that controls over human experimentation should be strengthened.

In 1971, the Department of Health, Education and Welfare (HEW) published a set of guidelines for all the research involving humans which it supports. The guidelines reflect the objectives spelled out in the Nuremberg

Code promulgated by the judges at the trial of Nazi war criminals. In short, they specify that three chief criteria must be fulfilled in any experiments on human subjects. First, the risks to the subject must be outweighed by the potential benefit to him or by the importance of the knowledge to be gained. Second, the subject must be fully informed of the possible risks, and he should give his consent without any coercion. And third, committees should be set up in institutions in which research on humans takes place to review the necessity for the research and to ensure that it is carried out ethically.

In theory, those applying for research grants from agencies in HEW must comply with the guidelines and, similarly, drug companies which apply to the Food and Drug Administration for permits to conduct drug trials should also comply with the guidelines. But, according to Dr Jay Katz of the Yale University School of Law and author of a book on *Experimentation with*

HEALTH RESEARCH

White House Lunacy

by our Washington Correspondent

THE Nixon Administration's plans for cutting back in some areas of biomedical research and for phasing out the NIH training grants and fellowships were described last week as "lunacy" by Professor James D. Watson, director of the Cold Spring Harbor Laboratory and professor of molecular biology at Harvard University. Testifying at the Senate Health Committee hearings on human experimentation, Watson also castigated the Administration for concentrating on research likely to have a quick payoff at the expense of more basic research. "This way of proceeding," he said, "represents a puerile understanding of both how good science is done and how its discoveries have been directed toward human application."

The object of Dr Watson's remarks was the Administration's budget for 1974, which proposes cutbacks in funding for every institute in the National Institutes of Health except the National Cancer Institute and the National Heart and Lung Institute, and the phasing out of all grants and fellowships administered by the NIH for training new researchers.

But Watson was not alone in his concern, for no less an authority than Dr Michael DeBakey, the renowned Houston heart surgeon, and Dr Lewis

Thomas, dean of the Yale School of Medicine, told the subcommittee of their misgivings. And Senator Edward M. Kennedy, the subcommittee's chairman, did not miss the opportunity to criticize the Nixon Administration, promising that he would do what he can to restore some of the money.

But it is not simply the cutbacks that concern Dr Watson, for he also expressed strong reservations last week about the trend towards more targeted research and in particular the use of contracts instead of grants for scientific programmes. He pointed out that "almost every important new discovery comes from someone under thirty-five and who at the moment of his breakthrough is essentially unknown to the outside world", and such people are thus unlikely to receive contracts "from a government that looks with distaste on the unpredictable".

As for the phasing out of training grants and fellowships, Watson predicted that "not only will all the money be tightly held by middle-aged entrepreneurs, but the science itself will have for the most part to be done by an age-group not noted for working into the night". Asked by Kennedy where the Administration gets its advice for the plans for biomedical research, Watson said that none of his colleagues supports the plans, and that the National Cancer Board, the chief advisory body for cancer research of which Watson is a member, "is not listened to".

Human Beings, although the guidelines "have provided some significant controls over research practices . . . they are inadequate and . . . the problems remain unsolved".

Those sentiments were echoed by several other witnesses at the hearings, and in particular by Dr Bernard Barber, chairman of the Department of Sociology at Columbia, who outlined the results of a survey of some 350 medical researchers engaged in 424 different studies involving human subjects. Dr Barber found that information supplied by the researchers themselves indicated that eighteen per cent of the studies involved more risk than benefit for the subjects, and even after the possible long-term benefits to society were included in the analysis, 8 per cent of the experiments involved more risk than benefit. Moreover, 9 per cent of the respondents in the survey volunteered the information that their research had not been subjected to peer review.

What steps should be taken to tighten control over human experimentation? Both Dr Barber and Dr Katz suggested that Congress should pass legislation setting up a board with authority to regulate at least federally funded research involving human subjects. Last year, the Senate passed a resolution sponsored by Senator Walter Mondale calling for a commission to study and make recommendations in the general area of medical ethics, but the proposal died in the committee rooms of the House of Representatives. Katz and Barber believe, however, that Congress should go one step further and set up a regulatory, rather than simply a study, organization.

The idea would be for the board to consist of people drawn from several disciplines and to include lay members. It would formulate detailed policies on such issues as the selection of subjects, informed consent and the application of risk-benefit criteria, and it would firmly guide the work of peer review committees in research institutions. Katz also suggested that the board should be independent of HEW so that it could have control over research sponsored by agencies such as Defense.

Other suggestions aired at the hearings included an immediate moratorium on research involving prisoners. Such experimentation is more extensive in the United States than in any other Western country, and it involves special issues such as the difficulty of obtaining genuinely free informed consent from a person who effectively has little freedom of choice. A number of serious abuses of medical ethics in prison research were detailed at the hearings last week (see box). It was also suggested that scientific journals should refuse to publish research results derived from studies involving unethical practices.

PRISON RESEARCH

Ethics Behind Bars

by our Washington Correspondent

IN April 1971 another priceless piece of information was added to the scientific literature with the publication of a paper describing the effects of vitamin deficiency in prisoners in Iowa State Penitentiary. To obtain the information, five prisoners were fed a diet deficient in vitamin C for up to three months, and the onset of scurvy was carefully monitored. The clinical signs included swollen and bleeding gums, loss of hair, haemorrhages in the skin and eyes, pain in the joints, loss of dental fillings and depression.

That is just one particularly outrageous example of research conducted on prisoners, described last week during hearings on human experimentation held by Senator Kennedy's Senate Health subcommittee — but the hearings also brought out the fact that the majority of preliminary drug testing in man in the United States is done behind prison walls.

According to Dr C. Joseph Stetler, president of the Pharmaceutical Manufacturers Association, about 70 per cent of Phase I drug tests — the preliminary safety studies which follow immediately after animal testing—are carried out on prisoners.

Dr Stetler defended the use of prisoners for drug testing on the grounds that the food and drug laws in the United States require extensive clinical trials of drugs before they can be approved, and that prisoners provide an ideal test group because of their particularly well controlled environment and diet. He also maintained that tests on healthy subjects are better, from both a scientific and ethical point of view, than trials on sick people. In many European countries, including Great Britain, where clinical trials are often carried out just on the sick, prisoners are seldom if ever used and Dr Stetler even went so far as to say that such testing is less scientifically rigorous.

Scientific justification and good medical practice apart, the drug companies also have a financial incentive to use prisoners for their testing. A typical payment to a prisoner for taking part in a drug trial is about $20 or $30 a month, which is less than one tenth of the going rate outside the prisons. Moreover, because a prisoner is less able to exercise his legal rights, the cost

of claims for damages is likely to be smaller.

Why do prisoners consent to the use of their bodies for the testing of new drugs? Therein lies the chief ethical question posed by prison research. Although low in comparison with fees outside, the $20 or $30 a month provides a great financial incentive to a prisoner who would normally earn only between $2 and $10 a month on regular prison duties. Moreover, the promise of escape from the tedium of prison life and the fact that a prisoner has little chance to exercise free will in prison surroundings also contribute to his decision ·to take part in trials.

With such incentives, and with such constraints on prisoners, are they in a position to give their consent to taking part in medical experiments freely, and with full understanding of the possible risks? Several·witnesses at the hearings last week said that they believed not, and some recommended than an immediate moratorium should be placed on medical research involving prisoners.

Others, particularly the representatives of the Pharmaceutical Manufacturers Association, however, said that they believe that existing guidelines for the conduct of research on human subjects are sufficient to ensure good medical practice, provided that they are rigorously enforced. Drug trials involving prisoners are regulated by the Food and Drug Administration, which must ensure that the trials are carried out in accordance with the Department of Health, Education and Welfare's guidelines for human experimentation, and similarly, other medical research on prisoners funded by the federal government should conform to the guidelines (see accompanying article). But it came out in the hearings that the FDA does not have a full record of drug trials carried out in prisons, and that in any case such information would not be available to the public because it would involve trade secrets.

If a moratorium were imposed on prison research, where would the drug companies find their volunteers? Dr Capron suggested that they should look to educated people outside the prisons, who are better placed to evaluate the risks involved in, and the justification for, such experiments. And Miss Jessica Mitford, the author came up with the novel suggestion that since the stockholders of drug companies stand to benefit most from the development of new drugs, they should volunteer.

But other witnesses suggested that no new controls are necessary. As far as the right of a physician to prescribe drugs for unapproved uses is concerned, for example, Dr William Barclay, executive vice-president of the American Medical Association, argued strongly for freedom. And Dr C. Joseph Stetler, president of the Pharmaceutical Manufacturers' Association, said that no new controls are needed to guide drug trials since the present HEW guidelines are adequate if effectively enforced.

Senator Kennedy, for one, seemed convinced, however, of the need for tighter regulation of human experimentation. He took representatives of the AMA to task for failing to provide leadership in ensuring that medical experimentation is carried out ethically, and labelled many of the incidences of abuse revealed during the hearings as "utterly outrageous". Legislation bearing his imprint can be expected.

WEATHER MODIFICATION
FAS Wants the Facts

by our Washington Correspondent

THE Federation of American Scientists has called upon President Nixon to release the facts concerning US weather modification activities over Vietnam during the war, and it has also called for an international treaty banning the use of weather modification as a weapon of war. At a press conference last week, Herbert Scoville, Jun., former deputy director of the CIA, and Gordon J. F. MacDonald, who until late last year was a member of the Council on Environmental Quality, speaking for the FAS, charged that the United States has used weather modification in the Indochina war, at least experimentally.

To back up that assertion, Dr MacDonald cited a passage in the Pentagon Papers which described "Operation Popeye"—an experimental programme which enhanced rainfall over Laos in 1966. The FAS in a press release also cites the fact that on September 8 last year a commercial weather modification firm filed suit against the federal government, claiming $95 million because the Pentagon had used a cloud-seeding device in violation of the firm's patent rights. Moreover, the federation points out that Melvin Laird, then Secretary of Defense, denied in testimony before Congress last year that weather modification had been conducted over North Vietnam, but pointedly omitted to mention the rest of Indochina.

In calling for an international treaty banning weather modification in warfare, the FAS suggests that such techniques would be "an opening wedge to the use of climate modification, the inducement of earthquakes and other

still more terrible weapons. We see geophysical warfare as a Pandora's Box, to which the seemingly inoffensive weather modification may be the disastrous key". Senator Claiborne Pell, together with 18 colleagues, has introduced a resolution into the Senate calling for an international treaty on this topic.

INDUSTRIAL RESEARCH
Optimistic Forecast

by our Washington Correspondent

THE National Science Foundation has forecast that industrially funded research and development will increase by 22 per cent between 1972 and 1975, rising from $11,400 million last year to $14,000 million by the middle of the decade. Based on a survey of projections made by the managers of research and development in 55 of the largest US corporations, the NSF forecast also suggests that industrial employment of scientists and engineers will increase by about 10 per cent over the same period.

The optimistic forecast given to the NSF by industrial executives "reflects a generally optimistic view of the economy", the foundation's report notes, and it is tied to expected increases in corporate earnings. During the late 1960s and early 1970s, corporate earnings declined, and companies tended to cut back in areas which would have little short term effect on profits—administration, marketing and research and development were prime candidates for the axe, the forecast suggests. The knife was not, however, applied with equal force to all items of research and development because applied research was allowed a moderate increase, while basic research was generally held back.

For the next few years, however, the National Science Foundation predicts that industrial funds for basic research will increase from $520 million last year to about $650 million in 1975. Of the 47 companies which offered forecasts, only one predicted a decline in spending on basic research, 13 predicted increases of up to 15 per cent, 22 reckoned they would spend between 16 and 35 per cent more, six forecast increases between 36 and 50 per cent, and five said they expected to increase spend-

ing on basic research by more than 50 per cent. The breakdown by industry is shown in Table 1.

The NSF forecast also suggests that many companies have consolidated their research and development operations during the past few years by centralizing the entire research effort, and thereby saving on such costs as library facilities and testing facilities. Moreover, although most of the company officials who responded to the survey said that expenditures required to reduce pollution have not had much effect on basic research spending, "a few of the companies noted that a significant proportion of their basic research programs was devoted to pollution control".

But the report is not entirely optimistic about expenditures on basic research, for it is pointed out that "there appears to be some disagreement regarding the value of basic research. Some companies, although continuing to perform basic research, question whether the results are worth the cost".

Short Notes
Earthquake Research

THE plan to transfer earthquake and geomagnetism research and monitoring facilities from the National Oceanic and Atmospheric Administration to the US Geological Survey (see Nature, **241**, 362; 1973) was still stalled at the end of last week, awaiting final approval from the Office of Management and Budget. The problem is that although the Geological Survey has agreed to pick up the research, which is being dropped by NOAA because of financial stringencies, and although the National Science Foundation has agreed to put up some of the funds, the USGS does not have enough positions allocated in the 1974 budget to staff the facilities involved. Unless OMB agrees to allow the survey to have more personnel, some activities may be dropped completely.

Saturn's Rings

A RADAR scan of Saturn has produced the surprising suggestion that Saturn's rings may be composed of chunks of solid rock, and not of dust, gas or ice particles, as widely believed. The scan, carried out by Dr Richard M. Goldstein and Dr George A. Morris, Jun., of the Jet Propulsion Laboratory, produced much stronger signals from the rings than expected. The echoes suggest that the material in the rings has rough, jagged edges, and that the chunks are probably at least a metre across. Fortunately, the Mariner Jupiter–Saturn mission, which is planned for launch in 1977, does not involve passage through the rings. The scan was carried out on NASA's 64 metre antenna at Goldstone in the Mojav Desert.

Table 1 Industrial Expenditures on Basic Research			
(Millions of current dollars)			
	1971	1972	1975 (est.)
All industries	$494	$520	$650
Drugs and medicines	95	105	140
Industrial chemicals	100	105	125
Petroleum	22	23	25
Electrical equipment	109	115	145
Aircraft and missiles	34	30	40
All other	134	142	175

NEWS AND VIEWS

A Classic Case of Irresponsibility

THE Metropolitan Museum of Art in New York has probably bought more than it bargained for with its recent acquisition of a splendid Greek painted vase of the sixth century BC. The museum by its purchase has undoubtedly fallen conspicuously below the standards of responsibility now expected of great archaeological institutions, and is in consequence likely to suffer a considerable dent in its prestige internationaly. The resulting publicity must be causing several museums to take stock of their purchasing policies just now.

The resentment widely felt by practising archaeologists at underhand dealings on the antiquities market must be viewed against the background of the world-wide pillaging of archaeological sites, which has increased dramatically and disastrously during the past decade. In Guatemala and Mexico, for instance, looters are using power saws to cut into pieces the wonderful sculpted stelai of the Mayan civilization. Merle G. Robinson has described (*Amer. Antiquity*, **37**, 147 ; 1972) cases where such sculptures have been split into pieces by fire to make them more portable, and was herself held at gunpoint by looters, posing as policemen, at the site of Itsimte. The resulting fragments, even when evidently sawn from a larger monument, command thousands of dollars on the art market.

The archaeological objection to such practices is not simply repugnance at theft and vandalism. The essential point is that monuments, objects and artefacts, however beautiful they may be as art works, lose most of their meaning when divorced from the context in which they are found. This applies to a Mayan stele ripped from the site to which it belongs (and to which its inscription refers), a coin in a Roman-British settlement located by a metal detector and dug up by "treasure seekers", or a Greek vase found in an Etruscan tomb with other objects and divorced from them for sale to a "connoisseur". In each case the irreparable loss is information. The destruction is going ahead at such a rate that there are now several aspects of man's past, formerly accessible to study, about which archaeologists will always be ignorant. To the irreparable damage in Mesoamerica must be added the archaeological rape of Cyprus, the ransacking of the Cycladic cemeteries of Greece, and especially the continuing plunder of the Etruscan cemeteries of Italy—the centre of an extensive antiquities trade for more than a century.

The archaeological world has now realized that policing the sites, although desirable, is not everywhere practicable. The solution must come from a new sense of responsibility among museums and private collectors. Pieces should be purchased only when their legitimate provenance is securely known, whether from authorized methodical excavation or from existing, recognized (and published) private collections. Anybody who buys antiquities in different circumstances is sustaining the market in plundered material. The Unesco draft convention on the safeguarding of archaeological sites (*Antiquity*, **45**, 246 ; 1971) sets clear guidelines, and lead-

ing institutions, such as the University of Pennsylvania Museum, and Harvard University (*Antiquity*, **46**, 90 : 1972) have drawn up conventions to ensure that their purchases do not directly or indirectly support looting or the illicit export of antiquities from the country of origin.

It is in this context that the Metropolitan Museum's purchase, for a reported $1,000,000, of an Attic red-figure vase, dated to about 510 BC and depicting a scene relating to the death of Sarpedon by the painter Euphronios, must be judged. It was acquired from an American dealer resident in Rome, who has in the past been charged with the violation of antiquities laws. He, in turn, claims to have obtained it from an Armenian antiquities dealer in Beirut (*The Observer*, February 25, 1973), but the vase has not previously been described, and there are grounds for suspecting it to have been illicitly excavated in Italy during the past five years.

That the museum should buy "the best Greek vase there is", in such circumstances and for a sum far in excess of any previously paid for a Greek vase, is scandalous enough ; reminiscent, indeed, of the purchase by the Boston Museum of Fine Arts of a golden treasure (see *Nature*, **232**, 515 ; 1971) which had obviously been illegally exported from some east Mediterranean land.

The attitude of the museum's officials is yet more shocking. Dietrich von Bothmer, the curator of Roman and Greek art and an internationally recognized authority, is credited in *The Times* of February 20, 1973, with the following statement:

> " 'I want to know whether it is genuine or fake. Its intermediate history is not important to archaeology. Why can't people look at it simply as archaeologists do, as an art object?' When asked whether he suspected that the vase could have been smuggled out of Italy recently, Mr von Bothmer answered: 'I am not suspecting anything. The thing I was concerned about was whether the object was genuine, whether the object was worth the money we spent on it'."

The pronouncement, echoing some of the less scrupulous nineteenth century "art lovers", that the circumstances of archaeological finds may be dismissed as "intermediate history", must rank as a classic of irresponsibility. More seriously, the admission of such a view—whatever the origin of the Euphronios vase itself—saddles the Metropolitan Museum of Art with a substantial measure of responsibility, albeit perhaps indirect, for the present looting and destruction of archaeological sites in the world at large.

The contumely of the scientific community in general, coupled with strong public pressure (for the scandal has been widely reported in the press), may yet bring the officials of the Metropolitan Museum to appreciate the magnitude of their present irresponsibility and the discredit which they bring upon the world of art scholarship.

From our Archaeology Correspondent

Sudden Events

THE importance of sudden events has become increasingly evident to astronomers in recent years. Perhaps such occurrences are noticed most commonly in some of the quasars. Typically what happens is that an intense component of radio emission, with a very small angular diameter, becomes visible for a period of a few months. During this time it contributes an appreciable proportion to the energy output of the whole quasar at radio frequencies. The radio emission at a given frequency first rises with time, reaches a maximum, and then decays; the higher frequency components achieve their maximum intensity before the lower frequency components. The whole effect can be explained beautifully on a model which was proposed by van der Laan several years ago. According to his ideas the radiation is generated in a giant bubble consisting of relativistic plasma mixed up with a magnetic field. As the bubble expands, the electrons lose energy and the magnetic field strength decreases. This gradually shifts to lower values both the frequencies at which the electrons emit most effectively and those at which the bubble is just transparent.

The model has one drawback, though. It says nothing about the way in which the relativistic plasma is given its energy in the first place. This is rather an important point, for the total energy required by the bubble depends very sensitively on the way in which it is started off. The early phases of its life are the most expensive in energy. But so far there are no observations of such a relativistic bubble in a quasar at the beginning of its life. In any case it may well be that the early phases of its evolution take place under conditions of such high density that it is impossible to observe directly just what is going on.

It is therefore fortunate that just over six months ago an outburst occurred in our Galaxy which looks very much like a small scale replica of such a sudden event in a quasar. The occasion was first observed on September 2, when the intensity of the radio emission from the X-ray source Cygnus X-3 suddenly increased by some orders of magnitude over its usual quiescent value. The subsequent events were comprehensively described in the October 23 issue of *Nature Physical Science*. It was found that the later evolution of the Cygnus X-3 outburst could be very well accounted for by the same model that van der Laan had proposed for sudden events in quasars (although the physical parameters such as magnetic field strength and total energy content had to be scaled down to the more modest proportions of this particular explosion). But it turned out that the observations made on the first day after the outburst did not fit the model too well. In particular there were oscillations in intensity at the higher frequencies that could not possibly be explained.

In an article on page 173 of this issue of *Nature* an attempt is made by Peterson to improve understanding of the early phases in the development of the bubble. He makes the modification that the relativistic plasma is not injected into the bubble all at once, but over a period of about a day. He postulates a particular form for the law governing the injection of plasma and then varies a set of parameters until he obtains the closest possible fit between his model and the observed evolution of the spectrum of the radio outburst. His conclusion is that the injection continued for about 30 h and that the minimum size of the bubble was about 10 AU.

Now this is most interesting, but also most tantalizing. How does all this agree with what is known about X-ray sources? Observations show that the X-ray emission from these sources often has quite short period oscillations, of the order of seconds. In the usual way one concludes that the underlying object must therefore be very compact; the only likely candidates are neutron stars or black holes. Somehow the release of the energy must have occurred in the underlying object. The energy was then propagated away from the source; later it was given to the radio bubble, which was observed after September 2. But neutron stars and black holes do not have dimensions as large as 10 AU; an estimate of 1 to 10 km would be much nearer the mark. There are therefore two problems: where did the energy come from, and how was it transmitted to the much larger region where the radio bubble began its existence?

Most probably the source of the energy is connected with the release of gravitational energy. It will be interesting to study how this happened, particularly if it turns out that the central object of Cygnus X-3 is actually a black hole. The transfer of energy, one would guess, must have occurred by some electromagnetic process, but under rather unfamiliar conditions. A reasonable picture might be as follows. Suppose that a mass of plasma falls towards a black hole or onto the surface of a neutron star. Suppose further that a quantity of magnetic flux is linked with the plasma. During the final stages of the collapse the magnetic dipole moment due to this flux will undergo rapid changes. One consequence is the emission of low-frequency electromagnetic radiation: the intensity of the emission increases up to the moment when the plasma gets lost in the black hole or the neutron star. If the plasma cloud has angular momentum the process may be augmented by the emission of low-frequency radiation from a rotating dipole, rather as is the case in some theoretical model of pulsars.

In either case one would expect a radiation field with characteristic frequencies in the region of 10 kHz. This radiation field has waves of low frequency but it carries much energy. Its mode of propagation through any ambient plasma is, however, not well understood; the waves have such a large amplitude that they cause large variations in the mass of the charged particles of the medium through which they are travelling. Any theoretical attempt at understanding this process leads at once to a difficult non-linear problem, whose solution is known in only a few special cases. But it does seem likely that in sudden events of this kind the relativistic electrons in the radio bubble have been energized by interaction with a set of low-frequency waves.

It is quite natural therefore that strenuous attempts should be made to understand these electromagnetic phenomena. The outburst of Cyg X-3 provides the best set of observations from which to derive data about the actual behaviour of such waves. The analysis by Peterson shows how one can extract much additional information from the records of the event.

F. D. K.

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The Problem of Pain

IT is relatively rare for scientific theory to lead directly to a new clinical procedure. The use of electrical stimulators on patients with intractable pain, however, is a case in point. These devices represent a radical reversal of the surgical approach to the problem of the patient who is left with severe chronic pain after damage to peripheral nerves or to the spinal cord. For whereas the aim of surgery is to destroy the nerve tract through which the pathological signals are transmitted to the brain, the idea behind the stimulators is to increase activity in the remaining normal nerve fibres.

This therapeutic approach arose from the Melzack-Wall gate control theory of pain, which states that the transmission of the sensation is controlled by the balance of activity in small diameter, slowly conducting fibres and large diameter, fast fibres entering the spinal cord. According to gate control theory, tonic activity in the small fibres which mediate pain is normally blocked at the first synapse by the activity of the large fibres which mediate mechanoreception, as well as by descending fibres from higher brain centres. The blockage can be overcome by very intense stimulation of the small diameter afferents, such as that which would result from tissue damage (Melzack and Wall, *Science*, **150**, 971; 1965).

The electrical stimulators are designed to excite the large diameter fibres, which have a relatively low threshold, without increasing activity in the higher-threshold small fibres, and thus to close the spinal "gate". They can now be surgically implanted in patients in the form of radio receivers, either close to a deep peripheral nerve or on the dorsal columns of the spinal cord itself, where stimulation is presumed to activate large diameter afferents antidromically (that is, by firing the axons passing on to the brain backwards, to close the gate).

In the United States, several hundred of these devices are now in use, and trials have recently begun in Britain, notably at the Institute of Neurology in Queen Square. The results have been mixed. At best, a short period of stimulation at intervals brings the patient total relief from pain. At worst, it has no effect at all. As far as can be judged, the clinical results seem to justify further trials at least. But do they vindicate the theory on which the therapy is based?

First, what is the explanation for the persistence of the analgesic effect, sometimes for several hours, after stimulation has stopped? Wall and Sweet (*Science*, **155**, 108; 1967) have suggested that the spontaneous activity of the small fibres may take time to reopen the gate. This would be consistent with the theory, but is not specifically predicted by it. Second, what is the effect on normal pain—for example pinprick—of stimulating the large diameter fibres? Wall and Sweet tried this on themselves with external stimulators and reported that pinprick in the analgesic areas did not feel sharp, though ordinary nonpainful sensation was unaffected. The accounts of patients on this point, however, are often conflicting and the issue is clearly complicated by the subjective nature of such judgments.

Indeed, the subjective nature of pain itself tends to confuse discussion of its possible mechanisms. While nobody would now dispute that painful sensation is mediated by specific anatomical pathways, the uncomfortable fact remains that severing these pathways does not always relieve pain. The arguments reach their metaphysical zenith when the surgeon, as a last resort, cuts the pain-carrying fibres between the thalamus and the frontal lobes of the cerebral cortex. The patient still feels the pain, but it no longer appears to worry him. The surgeon has apparently succeeded in eradicating the affect: hardly an anatomical concept.

The great advantage of gate control theory is that it attempts to explain the phenomena in purely neurophysiological terms at a manageable level of the nervous system and is therefore potentially testable. Attempts to identify the neurophysiological substrate for gate-controlled pain perception have thrown up several candidates for the spinal pathway involved, and have led to arguments about the circuitry of the gate(s) which remain inconclusive.

Wall and colleagues (*J. Physiol.*, **199**, 51; 1968), recording from the axons in the dorsolateral tract (DLT) of the cat spinal cord, found that they were driven both by small nonspecific afferents and by large mechanoreceptor afferents, which produced the expected facilitation of transmission in the case of the first, and presynaptic inhibition in the case of the second. Other workers, notably Perl and his colleagues at North Carolina, have fixed upon different pathways in which a proportion of the fibres can be driven by afferents which seem to be specific to noxious stimuli, but which do not seem to be subject to gate control, or at least not in the manner proposed by Melzack and Wall.

Dr P. R. Burgess, of the University of Utah, described at a recent conference of the Society for Neuroscience in Houston a paradoxical system in which noxious stimuli apparently close the gate. Small fibres responding to noxious stimuli are presynaptically inhibited by large mechanoreceptor fibres, as predicted, but when the stimulus is increased to noxious intensities, instead of breaking through the inhibition, they are even more firmly inhibited.

The most recent of the putative pain pathways is proposed by Dr B. Pomeranz, on the basis of single unit recordings from the ventrolateral tract (VLT) of the spinal cord (*Brain Res.*, **50**, 447; 1973). Thirty per cent of the fibres recorded by Pomeranz responded to noxious stimuli only; transmission, however, was neither facilitated presynaptically by stimulation of small diameter afferents, nor inhibited by large diameter afferents. On the basis of the proportion of fibres driven by noxious stimuli, Pomeranz reasons that the pathway is likely to be involved in the transmission of pain, but there is no evidence that it is gate-controlled.

A recurrent difficulty with research on the neurophysiology of sensory afferents is that their responses are profoundly influenced by general factors such as the condition of the animal from which the recordings are made. Such factors have often been called to account for discrepancies in the findings of different groups working on the same systems.

There is no doubt that the theory of pain as proposed by Melzack and Wall has been the basis for fruitful experiment both in the laboratory and in the clinic. One of the consequences of the work inspired by the theory has been to show where the theory is incomplete.

BRAIN DEVELOPMENT

Cerebellar Guidelines

from a Correspondent

THE mammalian brain is a structure of such complexity that the discovery of the principles governing its development poses a major challenge to biologists. One particularly productive approach to this problem is that adopted by Sidman and his colleagues at Harvard University. They have been studying, in mice, the effects of single gene mutations on neural structure, concentrating particularly on the cerebellum. This part of the brain is a beautifully ordered neuronal structure which is closely implicated in the fine coordination and control of muscular activity. A mutant animal with an abnormal cerebellum displays characteristic signs of muscular incoordination, low tone in the muscles and frequently a tremor. The various types of mutant have acquired evocative names such as "reeler", "swayer", "staggerer", "weaver" and "nervous".

In a recent report Rakic and Sidman (*Proc. US Nat. Acad. Sci.*, **70**, 241; 1973) analyse the cerebellar defect in the mutant weaver. In the homozygous animal there is, by the age of three weeks, an almost complete absence of one cell type—the granule cells. In the adult cerebellum the granule cell lies beneath the layer of Purkinje cells —those large cells whose axons constitute the sole output from the cerebellar cortex. The granule cells receive their input from mossy fibres, one of the two types of afferent fibres to the cerebellum, and send their axons to specialized spines on the dendrites of Purkinje cells. The granule cells are thus an essential link in one of the principal neuronal circuits of the cerebellum and it is not surprising that in their absence gross signs of cerebellar dysfunction are apparent.

What is the cause of the granule cell death in homozygous weaver mutants? Is the demise of the granule cell a primary effect of the defective gene or a secondary phenotypic expression of some more elusive primary genetic effect? During normal development the precursors of the granule cells travel over the surface of the brain to the surface of the cerebellum, where they then undergo massive proliferation. The daughter granule cells then migrate from the cerebellar surface through a dense meshwork of cells and cellular processes to assume their adult position deep in the cerebellum. In homozygous weaver the granule cells die at the cerebellar surface and hence no migration takes place. Rezai and Yoon (*Develop. Biol.*, **29**, 17; 1972) demonstrated that in weaver heterozygotes the granule cells proliferate normally but the daughter cells migrate

more slowly to their deep position. They suggested that in the homozygote cell death is secondary to a failure of migration rather than the reverse.

Rakic (*J. Comp. Neurol.*, **141**, 283; 1971), in an elegant electron microscope study of the developing monkey cerebellum, showed that throughout the entire extent of its difficult transcerebellar passage the migrating granule cell is intimately apposed to the process of a radially orientated glial cell (Bergmann cell). It was suggested that these glial processes act as necessary guidelines for the journey of the developing neurone, and in view of Rakic's discovery (*J. Comp. Neurol.*, **145**, 61; 1972) of a similar neurone-glial relationship in the developing cerebral cortex, it seems possible that such glial guidance is a fairly general phenomenon. Rakic and Sidman decided to investigate the relationship between granule cells and Bergmann glial cells in weaver mice to see if some abnormality in this relationship is the cause of the failure of the granule cells to migrate.

Rakic and Sidman found that in homozygous weaver mice the radial processes of the glial cells, although not entirely absent, are very rare. In the heterozygote, which does not display clinical symptoms, Bergmann glial processes are present but abnormal, the

distal processes being enlarged, irregular and vacuolated. This reduced effect in the heterozygote is part of the basis for the authors' conclusion that, although neuronal death is the most prominent and clinically relevant phenotypic expression of the weaver mutant, the Bergmann glial abnormality may actually be closer to the primary cellular target of the *wv* genetic locus.

The importance of normal cell migration in brain development is also demonstrated in "reeler" mice where defective migration leads to disordered neural structures. In reeler, however, it is proving more difficult to identify the primary genetic defect (Caviness and Sidman, *J. Comp. Neurol.*, **145**, 85; 1972; and **147**, 235; 1972). In "staggerer", on the other hand, the phenotypic expression of the defect consists of the absence of a specific synaptic relationship, that between the granule cell and the Purkinje cell dendrite. All other cerebellar synaptic relationships are present. Sidman argues that the primary defect, in this case, lies in the Purkinje cell itself.

A potentially very powerful complementary approach to cerebellar development is offered by Altman and Anderson (*J. Comp. Neurol.*, **146**, 355; 1972). Controlled X-irradiation at particular post-natal periods can destroy selectively certain neuronal populations

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What is the Origin of RD114 Virus?

RD114 VIRUS has attracted much attention recently because it has the characteristics of C-type RNA tumour virus and is released from human tumour cells, albeit human cells that have been passaged *in vitro* and in a foetal cat. The central question, of course, is what is the origin of RD114 virus? Is it a cat virus that infected the human cells during their passage in the kitten, or is it a human virus the replication of which was induced by the passage of the human cells in a kitten?

As has been shown by McAllister and his colleagues, who discovered RD114 virus, and by others, who have helped to characterize it, the antigens and the reverse transcriptase of RD114 virus particles are not closely related to their counterparts in either primate or feline C-type viruses. In an attempt to rule out the possibility that RD114 virus is merely feline leukaemia virus modified by passage in human cells, McAllister *et al.* performed the set of experiments that are reported in *Nature New Biology* next week (March 21).

McAllister *et al.* infected human RD cells, that do not release any virus, with either feline leukaemia virus or the Kirsten strain of murine sarcoma (this latter virus was obtained from rat cells and it grows well in both rats and human cells) and then assayed various

properties of the progeny virus particles to see if they had been modified by passage in the human RD cells. McAllister *et al.* also investigated the properties of the infected and transformed RD cells. As far as could be judged from the results of a variety of tests, feline leukaemia virus particles from infected RD cells were identical to feline leukaemia virus particles from cat cells. Likewise the Kirsten murine sarcoma virus was not detectably altered by passage in RD114 cells. This indicates that RD114 virus is distinct from feline leukaemia virus and it is not simply a feline leukaemia virus somehow modified by passage in RD human cells.

McAllister *et al.* hint at the possible origin of RD114 virus. Apparently Todaro and his colleagues have induced from cat cells a virus closely resembling RD114 virus. It may be therefore that RD114 virus is a feline C-type virus quite distinct and unrelated from the already characterized feline sarcoma and leukaemia viruses. As they say, "The cat may be the first species found to have two distinct unrelated C-type viruses"; this is interesting but is also a great disappointment for anybody who hoped that RD114 virus might be the first human C-type virus to have been isolated.

and the effects on cerebellar organization of the deletion of different cell populations by experimental or genetic means can be compared. These on-going studies are providing invaluable insights into the mechanisms of brain development.

PROTEINS

Sifting the Subunits

from our Molecular Biology Correspondent

THIS week some *bonnes bouches* for collectors of the odd in the way of protein structures. Some proteins, on no very obvious teleological grounds, exist under physiological conditions in very large aggregates, containing many subunits. One of the first cases to be recognized was haptoglobin, a serum globulin, which has the function of absorbing any haemoglobin that is released into the plasma. There are three familiar genetic variants of human haptoglobin, one of which (Hp 1-1) is electrophoretically homogeneous, whereas the others, Hp 2-1 and Hp 2-2, take the form of an apparently limitless series of components of progressively lower mobility in the electrophoretic gels. More than a dozen zones can often be resolved, and these are now recognized as a set of linear polymers, which can be separated on denaturation and reduction into two types of chain, α and β, the α chain being characteristic of the haptoglobin type, the β chain common to all three. Just what the relation is between the members of the family of oligomers—for example, whether they are built up by successive addition of $\alpha\beta$ units, or of tetramers, or, as has been suggested, by repeated dimerization—has hitherto been in doubt. Now, however, Fuller *et al.* (*Biochemistry*, **12**, 253; 1973) seem to have settled the question.

Their preparation of haptoglobin 2-2 showed fourteen resolved zones in polyacrylamide gels and the first eight of these were isolated by preparative electrophoresis. In the absence of a reducing agent, the polymers do not dissociate in sodium dodecyl sulphate, and so detergent-gel electrophoresis could be used to give a first estimate of the molecular weights of the resolved members of the series. The first zone had a mobility corresponding to a molecular weight of some 200,000, which is consistent with an $\alpha_3\beta_3$ structure, the α chains with a molecular weight of 17,000 and the β chains 40,000. The apparent molecular weight increment between successive zones was constant, and corresponded to the addition of an $\alpha\beta$ unit at each step. The components from 2 to 5 were examined by sedimentation equilibrium, and the inferred molecular weights from the electrophoresis experi-

ments were found nearly enough correct. The stoichiometry was more firmly established by amino-acid analysis and by end-group determination. Both confirmed that α and β chains were present in equimolar concentrations in all cases. Now it has been known for some time that the chains of the basic $\alpha\beta$ unit are united by disulphide bonds, and Fuller *et al.* now also show that disulphide bonds likewise secure these units to each other in the polymers, because electrophoresis in the presence of very low concentrations of mercaptoethanol reveals the progressive degradations of polymer 5, for example, to a mixture of components 2 to 5, number 4 being formed first. The $\alpha\beta$ subunits do not come apart, and the α-β disulphide bonds can, it seems, be reduced only under more drastic conditions. Evidently, therefore, the components of the polymerizable genetic haptoglobin forms are assembled by linear addition from a pool of $\alpha\beta$ units.

In unfolding the absorbing story of the enzymatic control of glycogen metabolism, Krebs and his colleagues have paused to examine the structural character of the phosphorylase kinase, which is responsible for the conversion by phosphorylation, of glycogen phosphorylase *b* to phosphorylase *a*. The activity of the phosphorylase kinase is itself controlled by cyclic AMP-dependent protein kinase, which catalyses its phosphorylation. The phosphorylase kinase emerges as a complicated enzyme with some curious properties. In the first of a set of three articles, Hayakawa *et al.* (*ibid.*, 567) describe the isolation of the protein in a high state of purity, having eliminated an aggregated fraction present in earlier preparations. The enzyme, when thus purified, has a sedimentation coefficient of 26S and a molecular weight, by sedimentation equilibrium, of 1.3×10^6. In sodium dodecyl sulphate it dissociates, and gives rise to three components with apparent molecular weights of 118,000, 108,000 and 41,000, which are termed the A, B and C chains. From the apparent concentrations of these components, the authors infer that the

Structure and Activity of Juvenile Hormone

MANY attempts have been made during the past few years to define the molecular characters that determine the juvenile hormone activity of the rather diverse chemicals which can produce these morphological effects (*Nature*, **221**, 190; 1969). In the first place the molecule must be neither too long nor too short: active substances have about fourteen carbon atoms in the chain length. They must not be too polar, nor must they be wholly paraffinic. General molecular configuration determined by *cis* or *trans* bonding along the chain is highly important, but no molecular shape that gives predictable effects has been defined.

The problem is complicated by the diverse effects of synthetics in different groups of insects. Although the natural juvenile hormone as originally isolated from the cecropia silkmoth seems to have universally high activity, even the simple straight chain compound dodecyl methyl ether is quite active in Lepidoptera, though very weak in activity in other groups; and "juvabione", the methyl ester of todomatuic acid from balsam fir, which is intensely active in plant bugs of the family Pyrrhocoridae, seems to be without effect in any other insects.

In next Wednesday's *Nature New Biology* (March 21), Punja, Ruscoe and Treadgold report on a new group of non-terpenoid compounds, esters of chrysanthemic acid, which possess a high order of juvenile hormone activity. These also were found to be active only in the pyrrhocorid bug *Dysdercus*; but the communication brings out clearly

that activity is largely determined by the configuration at the C_1 end of the molecule where the most active mimics have a terminal carboxy alkyl or similar group conjugated with a double bond held *trans* to a long alkyl chain. As clearly shown in Dreiding molecular models the most active chrysanthemates, the principal cecropia hormone and juvabione all have closely similar configurations which are superimposable over this region (see figure). Extensive changes in other parts of the molecule seem to be much less significant.
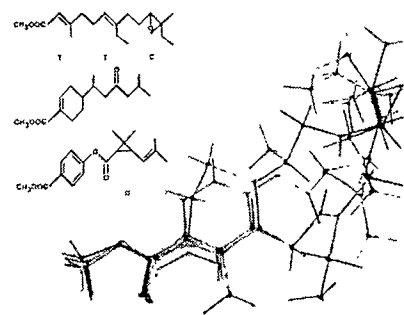
These results do not explain changes in overall and species-related activity which are associated with small variations in structure. There is no indication as to why the effect of chrysanthemates is specific for Pyrrhocoridae, nor for the increased activity which is conferred by a methyl side-chain at C_3 and by methyl (as compared with ethyl) esters. But the molecular models demonstrate the importance of the spatial relationships in the terminal groups of juvenile hormone and its mimics.

native enzyme has the structure $A_4B_4C_8$.

The A and B chains can be separated on a preparative scale from the smaller C chains by chromatography in sodium dodecyl sulphate solution (Hayakawa et al., ibid., 574) and the approximate molecular weights were confirmed by sedimentation equilibrium. The activation of the enzyme by incorporation of phosphorus from labelled ATP was found to implicate both the A and the B, but not the C, chains. Phosphorylation of the B chains occurred much more rapidly, but the activity continued to rise as incorporation progressed to the A chains. Activation can also be occasioned by exposure of the phosphorylase kinase to trypsin, and this again affects only the A and B subunits, both of which are broken down to fragments of lower molecular weight. Hayakawa et al. hazard the view that C, which is unaffected by any of these treatments, may be the catalytic subunit, which is regulated by A and B. Moreover, the trypsin-activated enzyme can, as Graves et al. (ibid., 580) report in the third article, be dissociated in the presence of ATP, by a slow process to smaller species, sedimenting at 9S and 16S, which possess activity, and in the smaller of which no part of the A subunit can be detected. The native, undigested, kinase cannot be made to dissociate under any but denaturing conditions, yet it seems that the very large cluster of subunits that comprises the native enzyme is not a condition for enzymatic activity.

Another curiosity, and the subject of a painstaking study by Roseman and his colleagues, is a bacterial protein involved in the transfer of phosphorus to lactose (Hays et al., J. Biol. Chem., 248, 941; 1973). The sites of phosphorylation are histidine residues. This protein has a molecular weight of 35,000 by sedimentation equilibrium, and has an unusual trimeric structure, being made up of three seemingly identical subunits of 12,000 molecular weight apiece.

TRANSCRIPTION

Elusive Sigma Factor

from our Cell Biology Correspondent

THE hopes of divining how RNA polymerase knows which DNA to transcribe and which DNA to leave untranscribed, that were raised among molecular biologists two and three years ago by the discovery of a subunit of Escherichia coli RNA polymerase called sigma factor, have slowly evaporated. And the article by Greenleaf, Linn and Losick in the current issue of the Proceedings of the National Academy of Sciences (70, 490; 1973) seems like a haunting voice from the past. During the heydays of sigma factor Losick and his colleagues confidently anticipated that during the sporulation of the bacterium Bacillus subtilis the change in pattern of transcription of the bacterial DNA would prove to result from changes in the RNA polymerase molecule, and at that time (1969) it seemed plausible to suggest that the sigma factor responsible for programming the transcription of genes expressed during the vegetative phase of the life cycle was replaced by a new sigma factor programming the transcription of different genes expressed specifically during sporulation.

Losick and his colleagues found that the vegetative sigma factor is indeed lost early during sporulation, a fact which could account for the turnoff of ribosomal RNA synthesis and the failure of the sporulating cells to support the growth of phage φe. They also found that one of the other polypeptide chains of the vegetative enzyme (the β subunit) is replaced by a smaller polypeptide during sporulation. Egged on by these discoveries, and in particular the loss of the vegetative stage sigma factor at the start of sporulation, Losick and his colleagues began to search for the putative new sigma factor characteristic of the enzyme in sporulating cells. The report in the February issue of the Proceedings describes the results of this search which, frankly, are disappointing.

If a new sigma factor is made during sporulation the obvious place to look for it is in the RNA polymerase from sporulating cells, of which the factor should be a component. Greenleaf et al. therefore prepared antibody against the core polymerase of vegetative cells (core polymerase lacks sigma factor). They then challenged RNA polymerase from sporulating cells with the anti-core polymerase antibody and found that a polypeptide with a molecular weight of about 70,000 co-precipitated with the polymerase from sporulating cells. Clearly this co-precipitating polypeptide not present in the vegetative core enzyme might well be a sporulation sigma factor. Greenleaf et al. therefore purified the 70,000-dalton polypeptide and established that it binds specifically to core RNA polymerase, a property which a putative sporulation sigma factor must have; depending on the conditions, 0.3 to 2 molecules of 70,000-dalton polypeptide bind to each core polymerase. Furthermore, this polypeptide first appears about 3 h after the start of sporulation and persists for about at least a further 3 h and it cannot be detected in RNA polymerase extracted from a mutant of B. subtilis, rfr10, which cannot sporulate and which is rifampicin resistant; cell extracts from this mutant also lack the 70,000-dalton polypeptide.

With such a body of circumstantial evidence it must have been hard for Greenleaf et al. to resist the temptation to send out for a corkscrew, but the celebrations would have been premature, for the last sentence of their report reads: "Attempts to demonstrate a role for the 70,000-dalton binding protein in the transcription of sporulation genes have not yet been successful."

Hatched from the Same Egg

THE evidence, based on sequence homologies, that several proteins have a common evolutionary origin brings a measure of conviction. Is the same true of non-translated gene products, namely ribosomal and transfer RNA? Mullins et al. have investigated this question and in next Wednesday's Nature New Biology (March 21) they report their comparison of the pre-modified sequences of non-informational RNAs including twenty-two tRNAs and 5S RNA.

Mullins et al. found that tRNA^{tyr} and tRNA^{gln} from Escherichia coli show a remarkable homology with 5S RNA from the same species and that several other tRNA sequences are only a little less homologous. Although several insertions and deletions are required to make these homologies manifest, they are apparently well above chance expectation. Nevertheless they show a peculiar pattern—which Mullins et al. term "displaced linear homology"—in that the first half of the tRNA sequences are homologous with the last third of the 5S sequence and the second half of the tRNA with the first third of the 5S. Moreover, the extra sequence of forty-one nucleotides at the 5' end of the precursor form of tRNA^{tyr} shows homology with the middle third of the 5S RNA sequence.

Mullins et al. interpret these results ingeniously, using the observation of Brownlee, Sanger and Barrell (Nature, 215, 735 ; 1967) that for E. coli 5S RNA the first nine residues show homology with the last nine and that region 10–60 is homologous with region 61–110; in other words, the molecule has a palindromic structure with the pattern ABBA. Mullins et al. postulate a proto-non-informational RNA consisting of about sixty residues with the pattern AB. They suggest that this gave, by processes of partial gene duplication, a sequence first with the structure ABB and then with the structure ABBABB. This, they suggest, gave by a similar process a sequence with the structure ABBA corresponding to 5S RNA and alternatively a sequence BAB, which after truncation would correspond to tRNA.

Until some direct evidence, either from *in vitro* experiments or from studies of mutant strains of *B. subtilis* carrying conditional lethal mutations in the structural gene specifying the 70,000-dalton polypeptide, is obtained the role of this polypeptide in the specificity of transcription during sporulation must remain uncertain.

LEUKAEMIC CELLS

Mutagenic Polymerase

from our Cell Physiology Correspondent

REPORTS about the physiology of various tumours and more particularly about the relationship between the host and the malignant cells are now legion, but although knowledge of the molecular biology of malignancy is fundamental to its control, information on this point is sadly lacking. It is true that many workers are investigating reverse transcriptase, but there are innumerable other facets of the molecular workings of these cells which also warrant study.

Springgate and Loeb have started on a new track, for they are now trying to determine whether DNA synthesis in malignant cells is less accurate than that of normal cells. The idea seems to be something of a shot in the dark, but in their recent report (*Proc. US Nat. Acad. Sci.*, **70**, 245 ; 1973) they show that the cells from four patients with acute lymphatic leukaemia have a DNA polymerase which is considerably less exact and makes a far greater number of mistakes when copying a template than does the DNA polymerase from normal human lymphocytes.

After removal of indigenous DNA the accuracy of synthesis was assessed by determining the proportion of radioactively labelled dGTP or dCTP incorporated during replication of a synthetic poly(dA-dT) · poly(dA-dT) template. The enzymes from leukaemic cells apparently lack the fidelity of those from normal lymphocytes, for the proportion of cytidine residues in DNA synthesized by polymerases from cells of patients with acute lymphatic leukaemia was some ten times higher than that made by DNA polymerases from normal lymphocytic polymerases the mic polymerases the level of errors lay between 1 in 250 and 1 in 850, with normal lymphocyte polymerases the error frequency was of the order of 1 in 2,000 to 1 in 30,000.

Control experiments indicate that the dCTP really is incorporated into the polynucleotide chain and is not merely attached to it non-specifically. In identical conditions the *Escherichia coli* enzyme was found to have an error frequency somewhat lower than 1 in 100,000 and that of T4 phage was in the region of 1 in 10,000 ; these values agree very closely with those found by

other authors. Other simple experiments also suggest that the observation is not an artefact, for the addition of cold, unlabelled dCTP to the nucleotide pool reduced the proportion of label incorporated into the freshly synthesized polymer and the requirements of the assay system for Mg^{2+}, template, nucleotides and enzyme are exactly the same for incorporation of both correct or incorrect bases. If the correct bases, dATP and dTTP, are labelled with ^{32}P and the incorrect base, dCTP, with ^{3}H, then the ratio between ^{3}H and ^{32}P remains the same, irrespective of both the amount of enzyme protein added to the reaction mixture and also to the time over which the reaction is measured.

Springgate and Loeb believe these experiments indicate that the incorrect dCTP is physically incorporated into the replicating polynucleotide ; much stronger support for this contention comes from two further experiments.

In the first experiment, caesium chloride density gradients showed the product of the polymerase reactions to band in the position expected for a poly(dA-dT)· poly(dA-dT) and, as would also be expected if the dCTP were an integral part of the molecule, ^{3}H-dCTP was found in exactly the same band. Again, if the freshly synthesized polynucleotide was labelled with ^{32}P-dTTP and ^{3}H-dCTP and then sequentially hydrolysed with snake venom phosphodiesterase the release of the two bases closely paralleled one another. These results indicate that the cytosine residues are incorporated into the DNA and that they are evenly distributed.

Apparently it was not possible to assess the extent of inaccuracy using a poly(dG) · poly(dC) template because the level of infidelity was too low to allow for accurate measurement. Results with the poly(dA-dT) · poly(dA-dT) template strongly suggest, however, that these acute lymphatic leukaemic cells

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Adherent Cells and B Cell Immunity or Tolerance

FOLLOWING the realization that many immune responses cannot be thought of in terms of the interaction of antigen with a single species of lymphocyte, cellular immunology has entered a more realistic but more complicated phase of analysis. Broadly there are three kinds of cell known to be involved—T lymphocytes from the thymus, B lymphocytes from the bone marrow (or bursal equivalent) and adherent cells which also derive from the bone marrow but which are probably macrophage-like cells rather than lymphocytes.

All three sorts of cell are thought to have specific and non-specific parts to play in an immune response. The favourite notion at present is that specifically-activated T cells synthesize both non-specific and specific factors as a result of contact with specific antigen. The specific factor, which is thought to be an immunoglobulin referred to as IgT, becomes bound to the surface of a macrophage where in turn it binds antigen. The antigen-IgT complex can stimulate B cells to produce the specific antibody. It is possible that the macrophage stimulated by antigen-antibody complexes and the activated B cell in their turn secrete non-specific and perhaps specific (in the case of B cells) regulators of the cellular consortium. In next Wednesday's *Nature New Biology* (March 21), Feldmann illustrates how the presence of an adherent cell can determine whether B cells are induced to synthesize a specific antibody by activated T cells or become specifically tolerant.

All Feldmann's results relate to experiments performed *in vitro* and carry

the limitation that the antibodies produced are IgM only. The crucial part of the study is that activated thymocytes in contact with DNP (dinitrophenyl) conjugated to the activating antigen (fowl gamma globulin) liberate into the supernatant a factor which can induce spleen cells previously primed *in vivo* to DNP flagellin and in the presence of DNP-POL (POL is polymerized flagellin) to produce anti-DNP antibody as measured by the Jerne technique. If adherent cells are removed from the spleen cell population before incubation with the supernatant, then little anti-DNP antibody but anti-POL antibody is produced. Feldmann's interpretation of this experiment is that IgT-DNP complexes can specifically immunize primed B cells when presented to the B cells by an adherent cell population, but can also specifically tolerize if they come in direct contact with the B cells.

Feldmann feels that these experiments have an *in vivo* parallel in those situations in which large numbers of activated T cells can suppress immunity. He distinguishes three phases in an immune response ; first, an exponential phase in which the amount of IgT is less than the number of receptors available on macrophages and therefore in the absence of unbound IgT-antigen complexes immunity will develop ; second, a plateau phase during which complexes and receptors are present in roughly equal numbers and in the absence of free complexes only immunity can result ; and third, a tolerance phase in which free IgT complexes are present and these effectively tolerize B cells.

do have some defect in their ability to replicate DNA with any accuracy. Does this result from errors in synthesis or through a failure of the nuclease to "edit" any errors introduced during DNA synthesis? Other questions concern the origin of the faulty polymerase. Is this of viral origin, or does it reflect the presence of an altered lymphocyte polymerase which is defective in base selection? On a more positive note, it is certain that such errors will enhance the mutation rate of these leukaemic cells and it is highly probable that this is responsible for the increasing variation which occurs during their proliferation.

The selective advantage which such random genetic mutation would confer on leukaemic cells is obvious, and what one now needs to know is whether DNA polymerases from the cells of other tumours show the same propensity for mis-replication. Is there, in fact, any relationship between mis-replication of DNA and a viral or non-viral origin of the malignancy?

EARTH MODELS

New Oceanic Model

from our Geomagnetism Correspondent

THE classical Earth models were seismically based on body wave travel-time data. In recent years, however, the range of geophysical information available to potential model makers has greatly increased, not least through the development of seismic arrays. This has led to several attempts to produce more realistic models. Haddon and Bullen (*Phys. Earth Planet. Interiors*, **2**, 35 ; 1969), for example, tried to update the Bullen-A model using eigenperiod data, although modes were only taken up to 44. Press (*Science*, **165**, 174 ; 1969 ; and others) generated by computer about 5 million random models which he reduced to a handful of successful models consistent with travel-time, eigenperiod and surface wave phase velocity data, although most of these were not entirely consistent with the group velocity data of both Love and Rayleigh waves. This fault was partly remedied by Kanamori (*Phys. Earth Planet. Interiors*, **2**, 259 ; 1970) who modified one of Press's most successful models, although even in this new model (5.08 M) Rayleigh wave velocities deviated from observation at periods below 150 s. Moreover, a predicted layer of very low density between 221 and 421 km may not be physically reasonable.

Appreciating the importance of group velocity data, Mizutani and Abe (*Phys. Earth Planet. Interiors*, **5**, 345 ; 1972) have now derived a new oceanic Earth model (designated OC–1) using a trial and error technique in conjunction with the equations of state for silicates and oxides, which are potential mantle

materials. The model has been designed to fit the Earth's total mass and moment of inertia, free oscillation periods for fundamental spheroidal and torsional modes up to 60, Love and Rayleigh wave phase velocities for purely oceanic paths in the period range 100 to 325 s, and Love and Rayleigh wave group velocities for predominantly oceanic paths in the same period range.

The chief characteristics of the model include a pronounced low-velocity layer between 70 km and 210 km (P wave velocity=7.70 to 7.74 km s^{-1}, S wave velocity=4.25 km s^{-1} and density=3,400 kg m^{-3}). Immediately above the low-velocity layer lies a region about 50 to 60 km thick with a high density (3,500 kg m^{-3}) and a high S wave velocity (4.72 km s^{-1}). Moreover, between 220 km and 340 km the S wave velocity has a negative gradient (thought to arise from an increase in the iron and pyroxene contents with depth) and there is a suggestion of chemical inhomogeneity with depth in the upper mantle.

The only problems of any significance (and that is debatable) seem to be that the predicted eigenperiods of the torsional mode are systematically higher than the observed ones by about 0.5 s, and the predicted Love wave phase velocities are about 0.01 km s^{-1} lower than the observed velocities at periods below 200 s. In this the Love waves and torsional modes differ from the Rayleigh waves and spheroidal modes for which prediction and observation agree. Mizutani and Abe note, however, that even these small discrepancies disappear if a small anisotropy of 0.7% is assumed to occur in the low-velocity layer. From the physical point of view, this is not an unreasonable supposition in a low-velocity layer caused by partial melting.

POLLUTION

Atmospheric Oxidation

from a Correspondent

IN a recent issue of the *Journal of the Chemical Society, Faraday Transactions I*, Cox and Penkett report their latest work on oxidation mechanisms in polluted atmospheres (**68**, 1735 ; 1972). They have carried out laboratory experiments in which mixtures of SO$_2$ and ozone are reacted with gaseous olefinic hydrocarbons. On injection of the olefin into the gas mixture the SO$_2$ is rapidly oxidized to form aerosol particles of sulphuric acid of submicron size, with a concomitant drop in the concentration of both ozone and SO$_2$ (see diagram).

The burning of fossil fuels at present introduces approximately 100 million tons of sulphur dioxide a year into the atmosphere. The fate of the gas after injection has received considerable attention of late, the chief impetus for these studies coming from the realization that increased levels of atmospheric SO$_2$ might have several harmful effects. These could include increased acidity of rain, and the formation of sulphate aerosols leading to decreased visibility in industrial areas where the input of man-made SO$_2$ is greatest.

Once in the atmosphere SO$_2$ may be directly adsorbed onto solid surfaces, taken up by plant leaves or, because of its considerable solubility and reactivity, dissolved in water droplets. Gaseous SO$_2$ may be oxidized to SO$_3$ by the action of ultraviolet radiation, atomic oxygen, oxygen or ozone, but such photochemical reactions in the gas phase are probably much less important

Structure in Solar Radio Bursts

THE solar radio bursts known as type V have been a puzzle since their discovery in 1958. At first, it was thought that their continuum radiation indicated a synchrotron origin, but more detailed observations suggested that Čerenkov radiation from coherent plasma waves is a better explanation, the waves being caused by electrons travelling at about 1/3 *c* which are magnetically trapped in the corona. In that case, harmonic structure ought to be detectable in the type V bursts ; in next Monday's

Nature Physical Science (March 19) Benz reports the detection of just such a structure.

The observation was associated with a radio flare which began on October 25, 1972. There is no doubt that this was a type V burst, says Benz, and it shows a distinct double structure (see figure). Because the shape of the two humps in the intensity curve is the same, and because two unrelated type V bursts are most unlikely to occur together in this way, it seems that this burst shows harmonic structure with a frequency ratio of 2 to 3.

If type V radiation is preferentially excited in a second harmonic, as has been suggested, the latest observations presumably include second and third harmonics—third order emission from the Sun has previously been found only in one U burst. What the theoreticians will make of this observation remains to be seen.
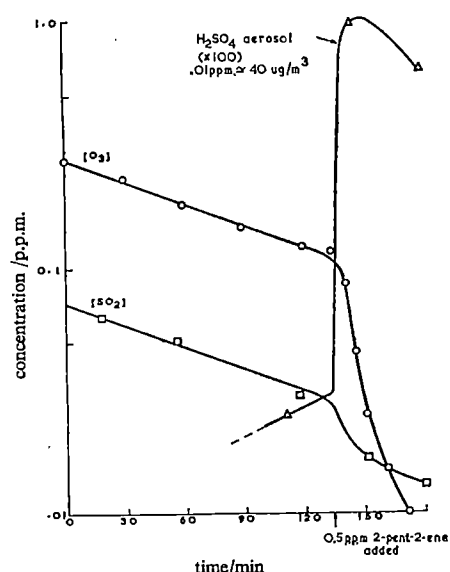
Curves of concentration against time for the reaction of ozone and SO_2, showing formation of H_2SO_4 aerosol on the addition of cis-pent-2-ene. (From Cox and Penkett, *J. Chem. Soc., Faraday Trans. I,* **68**, 1735; 1972.)

in the lower atmosphere than oxidation of dissolved SO_2 to sulphuric acid in water droplets. This is especially true if the droplets contain certain trace metals which act as catalysts for the oxidation. The droplets with sulphuric acid in them will subsequently react rapidly with any ammonium or sodium chloride in the air to form an aerosol of sulphate particles.

Because sulphur dioxide does not react directly with olefins, and the oxidation of SO_2 by ozone occurs only at a slow rate, Cox and Penkett conclude that all three components (ozone, olefin and SO_2) are necessary for rapid formation of the sulphuric acid aerosol.

Various olefins containing between four and six carbon atoms were used in the experiments, the rate of reaction being appreciably faster for internally unsaturated olefins (those in which the double bond is not at the end of the molecule). The rate of reaction is dependent on the concentration of both ozone and olefin, which are consumed in roughly equal amounts. Cox and Penkett consider two possible mechanisms for the process, both of which have the initial reaction of ozone and olefin to form an intermediate as the rate-determining step. In one the ozone bridges across the double bond of the olefin to form a ring complex, and in the other the ozone and olefin form a zwitter (or internal) ion. Whichever intermediate is formed it speedily oxidizes the SO_2 to SO_3 and is itself reduced to an aldehyde. Once produced, the SO_3 will rapidly react with water to form sulphuric acid, which subsequently nucleates to form the aerosol. From the laboratory experiments it seems that the rate of aerosol formation decreases with increase in

relative humidity. Cox and Penkett find no obvious explanation for this result, and conclude that its elucidation must await further information about the intermediate formed in the reaction of ozone and olefin and details of the aerosol formation process.

In the final section of their article Cox and Penkett discuss the application of the SO_2 oxidation rates determined in their laboratory experiments to the real atmosphere. Downward mixing of stratospheric ozone, followed by admixture with urban air containing SO_2 and olefins from fossil fuel combustion, is a possible route for sulphate aerosol formation by means of the ozone-olefin reaction. But because of the rather low concentrations of ozone and olefin in this situation (0.03 and 0.005 p.p.m. respectively) the rate of oxidation of SO_2 is only 0.1% h^{-1}. In polluted air the levels of ozone may be considerably higher because of photochemical formation of the gas *in situ* by reaction between NO_2 and hydrocarbons. In such environments ozone and olefin levels of 0.1 and 0.05 p.p.m. respectively are not uncommon and the rate at which SO_2 is oxidized to sulphate is about 3% h^{-1}. Thus in polluted air, where significant amounts of SO_2, olefin and ozone occur, the oxidation of SO_2 by way of a short-lived intermediate of the olefin-ozone reaction may well be important.

Progress with Lasers

from a Correspondent

AN interesting meeting on holography and laser applications in the analysis of displacement and strain was held at the National Physical Laboratory on February 7. There were nine speakers representing between them the National Engineering Laboratory, the National Physical Laboratory, University College, Swansea, Loughborough University of Technology and the Atomic Weapons Research Establishment (AWRE). It was very clear that the strongest interests represented were those of optics, and that the analysis of strain measurement by these methods still has some way to go. The challenge of most of the work discussed is to make it positively useful in real circumstances, but there were few examples of actual measurements of strain. Of the real applications mentioned, an important subdivision could be drawn between those optical techniques which are an alternative to existing methods and those which enable additional information to be obtained. It is the latter type which is most likely to make an impact on technological developments.

Dr J. M. Burch (NPL) was at pains to point out that holographic interferometry was invented simultaneously by several

Salic Bias of Continental Crust

WHY is it that continental alkaline provinces contain a far higher proportion of salic rocks than do corresponding oceanic areas? For example, up to half the volume of lava in a continental province may comprise rhyolites, phonolites and trachytes, whereas an oceanic island contains very little salic material. Moreover, why is it that in continental provinces salic intrusions are most frequently of central form whereas mafic intrusions are most frequently of dyke form?

In next Monday's *Nature Physical Science* (March 19), Gill proposes a hypothesis which gives plausible answers to both of these questions and which overcomes the principal objection to existing explanations (partial melting and magma stratification) for the salic bias of continents, namely, that such explanations do not actually differentiate between continents and oceans. In other words, although partial melting and magma stratification could lead to the presence of salic material in the continental crust, there is no obvious reason why oceanic crust should be excluded from the action of such processes.

Gill's new hypothesis stems basically from the expected disparity in the time

scales of crustal and mantle processes. The point here is that mafic dyking in alkaline provinces is clearly an intermittent process dependent upon crustal conditions, whereas there is no obvious reason why magma generation should cease just because and when crustal conditions are not appropriate to dyking. It is therefore logical to ask what happens to newly generated magma during periods of no dyking when access to the surface by way of fissures is not possible.

Density considerations suggest to Gill that when continental crust is not amenable to dyking, magma is at first restricted to depths greater than about 10 km where it cools, in time giving low-temperature residual liquids. Because of a relative lack of buoyancy, mafic components of the magma will be confined to this reservoir but the salic magma may rise by stoping and thus give upper crustal central forms. By contrast, oceanic crust offers much less restriction on dyking and so activity is predominantly basaltic. The critical difference between continental and oceanic crust, which leads to the salic bias of the former, is thus simply the different propensities to allow crustal extension.

workers and that both British scientists and American scientists can share that achievement. Perhaps the focal point for laser applications in engineering came with the international meeting in 1968 at the University of Strathclyde, where the engineering applications of holography formed the principal theme. At that time holography had been very widely applied to practically all types of engineering measurement. Some of these applications proved to be successful and work continued, but others fell by the wayside and it was somewhat disappointing on reflexion to see how little progress has been made in the applications field.

One of the chief things required of holography is information about how and why an object moves or how a displacement takes place. Such information is provided in terms of an interference fringe pattern, the interpretation of which has been the subject of much discussion in the past. The topic was again raised at this meeting and it now seems that adequate analysis and solutions are available; this should encourage would-be users to take courage and obtain a laser. The Loughborough group has taken a slightly different line in avoiding the analysis of complex interference patterns by changing the experimental technique to one which effectively uses the interference fringes as a linear scale. Apparatus for doing this was described and results shown from a video tape. The equipment itself is called the Electronic Speckle Pattern Interferometer (ESPI) and it was demonstrated by application to vibration visualization and to dynamic strain visualization in carbon fibre-reinforced plastics.

One application of holographic interferometry in which quantitative analysis of interferograms is not required is non-destructive testing (NDT). Some examples of this were provided by the National Engineering Laboratory where minute cracks are being detected in high-pressure gas cylinders. There is some difference of opinion as to whether the terms non-destructive testing or non-destructive evaluation should be used, but the issue is further complicated by experimental work at the National Physical Laboratory. Here they have shown by means of holographic interferometry that one's eyes bulge on being hit on the head with a hammer. (Safety helmets were worn for these experiments.) Other NDT applications mentioned include the testing of fabricated components for aircraft work and other sophisticated or high reliability applications. The Loughborough ESPI can also be used for such tasks.

Speckle pattern methods came in for considerable discussion involving the NPL and University College, Swansea,

in addition to ESPI. Although it is in many ways similar to holography, speckle pattern interferometry offers a greater degree of sensitivity control. Mr A. E. Ennos (NPL) has used this to desensitize a method of displacement measurement, and Mr A. R. Luxmoore (University College, Swansea) extended discussion on this theme. The apparatus for speckle pattern interferometry can be very simple when photographic recording is used. The work described used an ordinary 35 mm film camera and was stated to give minimal demands on laser coherence. In the case of photographic recording, results are often enhanced by a stage of optical filtering

following the test; very clear fringes are observed under these circumstances. If, however, rapid or on-line results are required there is only marginal advantage over holography.

The meeting was brought back to thoughts on holography by Mr M. R. Wall (AWRE) who shares a place with the early inventors of holographic interferometry. In many ways he set out to explode the myth that holography is for the specialist laboratory only, because in a few moments he explained how, with a pulsed laser, it is possible to record a holographic interferogram of a hot pressure vessel on site and also how to interpret fringes.

Plate Tectonics in Scotland

IN next Monday's *Nature Physical Science* (March 19), Garson and Plant offer a plate tectonic interpretation of the Scottish ophiolite sequences which is significantly different from that recently given by Dewey (*Scott. J. Geol.*, 7, 219; 1971). According to Dewey, the whole Caledonian orogeny was related to a consuming plate margin to the north of the Southern Uplands, with a northward-dipping Benioff zone along the Southern Uplands fault active between the Lower Ordovician and the Lower Devonian. But as Garson and Plant point out, there are several objections to this interpretation, the most general one being that the Southern Uplands fault seems to be too far removed to explain the ophiolite sequences in the Highlands to the north.

Garson and Plant thus propose a different pattern of development in which the Scottish Highlands mountain belt evolved in three principal episodes corresponding to the three "significant" belts of Alpine-type ultramafic rocks— the Moine, Dalradian and Highland Border Belts (see map), respectively. Thus, whereas Dewey's model envisages a long, passive sedimentation phase followed by a relatively short orogeny, Garson and Plant suggest progressive deformation and addition of continental material with an episodic movement of a consuming plate margin towards the south-east.

In the first of the proposed episodes (Morarian), the Alpine-type ultramafic rocks of the Moine belt were intruded into a eugeosynclinal sequence during a phase of mountain building in the Precambrian (750 to 800 million years ago). Garson and Plant suggest this to have been related to an oceanic plate underthrusting the continental margin at a time when the proto-Atlantic Ocean was closing. The second orogenic episode (Upper Dalradian), which began after the Morarian plate descent had stopped, took place at the edge of a new continental crust extended from its pre-

vious position by the addition of eugeosynclinal and miogeosynclinal sediments from the Morarian episode. At this stage (Lower to Upper Cambrian), the second ophiolite belt was intruded as a new phase of lithospheric descent took place, possibly indicating another closing of the proto-Atlantic Ocean.
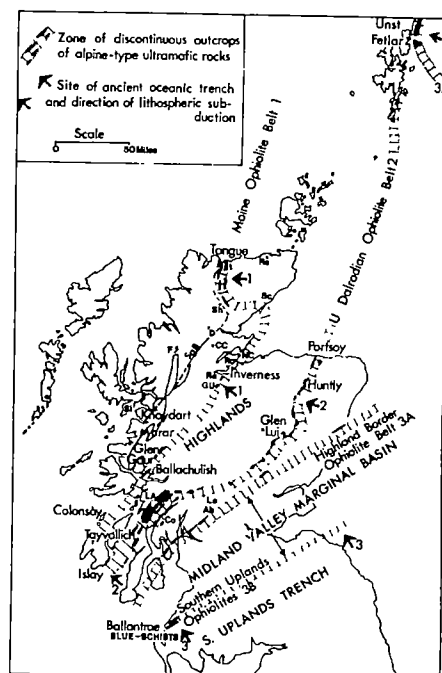
The third episode apparently continued the orogenic processes represented by the other two, leading to the emplacement of the Highland Border ophiolite belt during the lower Ordovician, although it is difficult to visualize in detail because of obscuration of the evidence by subsequent faulting and erosion. This only leaves the ophiolites of the Southern Uplands to be accounted for. According to Garson and Plant, the Midland Valley is symmetrical in that the two ophiolite belts which border it are of comparable age. They thus envisage that the Midland Valley originated as a marginal sea.

Linkage Analysis in Man by Somatic Cell Genetics

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Techniques for the study of somatic cell genetics, and particularly those involving the expression of enzyme markers in hybrid cells, have already made possible a large number of gene-chromosome assignments. Genetic and family studies, as well as cellular studies on recombination and gene transfer, promise more and quicker results in the future.

SOMATIC cell hybridization, first demonstrated by Barski et al.[1], was an important early step in the formulation of somatic cell genetic systems, allowing as it does the combination of genetically different genomes within a single cell. In a series of investigations Ephrussi and his colleagues showed that hybrid combinations could be obtained between the cells of different species[2], and that chromosomes of one or both parental genomes could be lost or segregated from the hybrid cell[3]. Weiss and Green[4] first demonstrated the practical application of somatic fusion-segregation systems for the purpose of gene mapping in man (see below). Other investigators have contributed useful procedures which enhance the formation of hybrid cells and their enrichment. These developments now allow a completely new cell culture approach to gene mapping in man.

Cultivation of Hybrid Cells

For the formation of hybrid cells the parental cells are mixed together and co-cultivated. Membrane fusion can be enhanced by treatment with inactivated Sendai virus[5,6] or with lysolecithin[7]. Fusion between two parental cells of different origins gives rise to a binucleate heterokaryon. Heterokaryons have a short life expectancy, and following their first mitosis, generally form mononucleated or hybrid daughter cells which contain chromosomes from both parental genomes. In many parental cell combinations, the hybrids have an infinite life expectancy and can be grown into large clonal cell populations. In man–mouse and man–Chinese hamster hybrids there is a unilateral loss or segregation of human chromosomes. The segregation of human chromosomes is variable in extent in different clones, and in many instances clones can be obtained which maintain for many generations a partial human chromosome constitution. Thus, it is possible in effect to sample different numbers and combinations of human chromosomes in a series of man–rodent hybrids of independent origin. Each clone represents a partial human karyotype superimposed on an intact mouse or Chinese hamster genome. The experimental isolation of partial human chromosome complements forms the basis of somatic cell linkage analysis.

Enzyme complementation has been used to enrich for hybrids in mixed populations of parental cels. Littlefield has shown that drug resistance mutant cell lines can be useful in this regard[8]. Mutant cell lines can be selected which are deficient in the enzymes hypoxanthine-guanine phosphoribosyltransferase (HGPRT) and thymidine kinase (TK) by exposing cells to the antimetabolites thioguanine and BUdR respectively. HGPRT deficient cells cannot incorporate hypoxanthine, whereas TK deficient cells cannot metabolize thymidine. If de novo synthesis of purines and pyrimidines is blocked by the antimetabolite aminopterin, cells become dependent for survival on exogenous hypoxanthine and thymidine. HGPRT and TK deficient cells are thus conditional lethal mutants which are killed by aminopterin irrespective of the availability of hypoxanthine and thymidine. The fusion of HGPRT deficient with TK deficient parental cells yields hybrid cells whose enzyme deficiencies are complemented and which can grow in nonpermissive selection medium containing hypoxanthine, aminopterin, and thymidine (HAT medium). Kusano et al. have shown that adenine phosphoribosyltransferase (APRT) deficiency mutations can be used similarly for hybrid cell selection[9]. Conditional lethal mutants other than those based on drug resistance can also be used for hybrid selection. Puck et al. have used nutritional auxotrophs with good results[10,11], and it is likely that temperature sensitive mutations can be used in the same way[12]. Moreover, it is possible to make use of conditional mutant established rodent cell lines in combination with diploid human fibroblasts or leucocytes which have low growth potentials in vitro[12,13]. One can select against the rodent parent using nonpermissive medium and against the human diploid parent by virtue of its inherently poor growth characteristics.

Conditional lethal cell mutants in rodent cell populations are extremely useful for genetic analysis. In nonpermissive conditions only hybrids which retain the complementing human gene will survive. Thus, if one forms hybrids between HGPRT deficient rodent cells and wild type human cells (HGPRT+), and cultivates them in HAT medium. only those cells which retain the human HGPRT gene will survive. Generally, the intact human X chromosome which carries the HGPRT gene is retained in the complemented hybrid. It is possible to conceive of a series of rodent cell lines each of which carry different conditional lethal mutations which are complemented by genes on each of the human autosomes and sex chromosomes. Such a panel of rodent cell lines would be extremely useful in mapping studies because each would produce hybrids in which the segregation of a specific human chromosome would be fixed. Conditional lethal mutants of this type are tabulated in Table 1. It should be pointed out that the drug resistance complementation systems also lend themselves to counter selection. Cells which retain TK, APRT, and HGPRT activity are susceptible to the antimetabolites BUdR, fluoroadenine, and thioguanine, respectively[8–10]. Thus it is possible to use these agents in permissive medium to select against hybrid cells which have retained human chromosomes 17, 16 and X.

Table 1 Conditional Drug Resistance and Nutritional Auxotrophic Genetic Markers

Rodent mutation	Rodent parent	Complementing human enzyme	Human linkage unit
HGPRT deficiency	Mouse	HGPRT+	X
TK deficiency	Mouse	TK+	17
APRT deficiency	Mouse	APRT+	16
Glycine A auxotroph	Chinese hamster	Serine hydroxy-methylase	12
Adenine B auxotroph	Chinese hamster	Unknown	4 or 5

Rodent–Human Hybrids

In rodent–human hybrids, the human chromosomes are unilaterally segregated, both homologous human and rodent enzymes are expressed and can be identified, and human and mouse chromosomes can be discriminated and accurately identified on an individual basis. These hybrids are therefore particularly suitable for human gene linkage analysis.

The loss of human chromosomes from mouse–human and Chinese hamster–human hybrids is well documented, but the mechanism of loss is poorly understood. Preferential loss of human chromosomes in rodent X human hybrids, irrespective of the origins of the parental cell populations, is the rule, and only one possible exception has been reported[15]. A mechanism of loss suggested by Handmaker (personal communication) is that human chromosomes cannot attach efficiently to the hybrid spindle apparatus and thus have higher incidence of loss. Another possibility, which is not necessarily incompatible with this, is a mechanism of segregation based on random non-disjunction of mouse and human chromosomes in combination with the preferential selection of hybrids which possess partial human karyotypes[16]. Nabholz et al.[17] have suggested that chromosomes are lost by two temporarily distinct processes. Early loss, possibly during the first several mitotic divisions after fusion, can result in the abrupt loss of a few or many human chromosomes. Late loss is characterized by slow progressive loss in some instances over many cell generations. Nabholz et al.[17] have also presented evidence that human chromosomes are segregated non-randomly into hybrid clones. Preliminary results in our laboratory, based on twenty-eight independent hybrid clones, indicate a very low frequency of retention of human chromosome 9 (7%) compared with the overall frequency of human chromosome retention (29%). It has been reported that hybrids with two rodent genomes (2s hybrids) retain more human chromosomes than 1s hybrids[15]. The relationship between rodent and human chromosome number is significant and should be resolved, because it is fundamental to the problem of chromosome segregation.

The amino-acid constitution of homologous enzymes between man and rodents generally differs to some degree as a result of evolutionary divergence, and it is generally possible to detect these differences by electrophoretic procedures. There is thus a very large potential catalogue of genetic markers in the rodent–human cell hybrid system, limited only by the development of adequate test procedures. A compilation of isozyme procedures has been reported by Ruddle and Nichols[18].

It is important for genetic testing that the enzyme markers be constitutive—that is, they must invariably be expressed if the corresponding structural gene is retained in the hybrid. Facultative markers are defined as those markers which are subject to modulation and which may not be expressed even if the corresponding cistron is present. It is very difficult to define phenotypes as being absolutely constitutive or facultative. Generally speaking, enzymes which are expressed in all cell types in vivo and which contribute to vital metabolic pathways are termed constitutive, whereas enzymes which are restricted to one or a few specialized cell types and which do not participate in vital metabolic activities at a cellular level are termed facultative. Good evidence exists for the modulation of certain facultative functions in hybrid combinations between parental cells of different epigenetic types[19]. This necessarily complicates the linkage analysis of such phenotypes. Phenotypes classified as constitutive may under certain conditions be modulated. For example, hybrid clones have been recovered by Ricciuti[20] which possess normal C-7 human chromosomes, but which do not express detectable levels of mannose-phosphate isomerase (MPI) activity. Linkage analysis in other cell hybrids shows a strong correlation between C-7 and MPI. I have concluded that MPI may represent a partially constitutive phenotype. Such phenotypes pose problems for linkage analysis, but they also provide useful material for studies on phenotype modulation.

Cytological Identification of Chromosomes

It is now possible to identify all of the chromosomes of the Chinese hamster, laboratory mouse, and man by cytological procedures. Caspersson and co-workers[21] have shown that quinacrine binds differentially to specific regions of the human chromosomes, and that each chromosome possesses a unique banding pattern. Mouse chromosomes are similarly unique and the banding patterns have now been correlated with known murine linkage groups[22]. Giemsa banding procedures provide results comparable with those of quinacrine[23]. Pardue and Gall have introduced an in situ annealing technique which makes possible the localization of highly redundant DNA in mouse and human chromosomes[24]. Purified isotopically labelled redundant DNA is annealed to intact chromosomes which have been pretreated with DNA denaturation agents. The labelled redundant DNA is hybridized to complementary DNA in the chromosome, and its location revealed by autoradiography. Pardue and Gall have shown that the murine redundant DNA (satellite DNA) is restricted to the centromere regions and that denaturation followed by Giemsa staining reveals positively staining, constitutive heterochromatin regions in the chromosomes. Arrighi and Hsu[25] have adapted this method to the analysis of human chromosomes and subsequent studies have shown a correspondence between constitutive heterochromatin and redundant DNA[26]. Human and mouse satellite DNA are specific and do not cross react. It is thus possible by hybridization in situ to distinguish human and mouse centromeric regions, which has proved useful in the detection of human–mouse chromosome translocations[27] (see below). Several laboratories have reported evidence indicating that the centromeric constitutive heterochromatin in man has different physical properties unique for several of the human chromosomes[28].

Assigning Genes to Chromosomes

Linkage of enzyme phenotypes can be inferred from their concordant segregation. The human chromosomes maintain their integrity for the most part, seldom undergoing rearrangement or deletion, and the concordant segregation of markers thus provides evidence for their location on the same chromosome irrespective of map distance. It is therefore appropriate to employ the term "synteny" coined by Renwick to signify merely localization on the same chromosome. Synteny testing is performed by comparing the segregation pattern of all markers in all pairwise combinations. The synteny test is less biased if performed on

clones of independent origin and the detection of valid syntenic relationships is enhanced by using clones derived from separate hybridization experiments, using different hybrid combinations. This generally entails computer analysis because of the number of clones and markers involved.

Individual genes or syntenic genes can be assigned to specific chromosomes by tabulating the human chromosomes in each of the clones and correlating them with the enzyme markers. The concordant presence or absence between a chromosome and a phenotype provides evidence for the assignment of the gene governing a particular phenotype to a specific chromosome. Twenty to thirty metaphases are analysed per clone by means of quinacrine banding, Giemsa banding, or constitutive heterochromatin staining techniques. Identification is enhanced if cells are first photographed by quinacrine fluorescence and then by constitutive heterochromatin staining procedures.

It is frequently possible to strengthen the assignment of a gene to a particular chromosome by correlating the frequency of a particular chromosome within a clone with the intensity of expression of an assigned phenotype(s). Discrepant clones of two classes can occur, however. In the first, presuming a valid assignment, the chromosome cannot be detected but the phenotype is present. We have demonstrated cryptic, rearranged chromosomes in a number of such instances which explain an apparently discordant chromosome/gene relationship[29]. A second type of discrepant clone involves the presence of a specific chromosome, but the absence of its corresponding phenotype(s). Clones of this type are difficult to explain, but could involve subtle rearrangements in chromosome structure, gene mutation, modulation of gene expression, or technical failure in phenotype detection.

It is possible to assign genes to particular regions of chromosomes such as chromosome arms, or band regions as defined by particular staining reactions. This can be accomplished by making use of chromosome rearrangements such as translocations and deletions in the human parental cell population or by making use of spontaneous chromosome rearrangements which are generated in the hybrids. Translocations of chromosomes to or between chromosomes X, 17, and 16 are useful because these chromosomes possess selectable loci. A number of translocations affecting the same chromosome but with different breakpoints can be used to restrict the localization of genes. For this purpose it will be particularly useful to characterize and store in central repositories all detected human translocations, to serve as a library of rearrangement products for future somatic cell gene mapping. Programs of human mutant cell banking are now being formulated in several countries. An example of regional linkage assignments based on translocations in parental cells is cited below for the X chromosome.

It is also possible to make use of spontaneous, sporadic chromosome rearrangements which occur in hybrid cells to fix the location of genes within subregions of particular chromosomes. Human chromosomes within hybrids may undergo rearrangement and even translocation to mouse chromosomes[29] and it has been possible to make use of such rearrangements to restrict the localization of the thymidine kinase gene to the long arm of human chromosome 17[29]. The translocation of human chromosome segments to the mouse chromosome set is significant from a genetic point of view because it may serve to restrict the further segregation of human genes involved in the translocation. It is conceivable that treatment of parental cells or hybrids with physical or chemical chromosome breaking agents could be used to induce chromosome rearrangements. Enrichment procedures could be devised to select particular classes of rearrangement products. Such systems could be used to increase the resolution of subregional chromosome gene assignments.

Known Human Linkage Groups

A significant number of syntenic relationships and chromosome assignments has been established by somatic cell genetics. A survey of the current linkage information is presented below for each of the human chromosomes in turn. The results are also summarized in Table 2. For chromosome 1, Van Cong et al.[30] have reported a syntenic relationship between phosphoglucomutase-1 (PGM$_1$) and peptidase C (Pep C) using mouse–human hybrids. This synteny has been confirmed by Ruddle et al.[31]. Using Chinese hamster–human hybrids, Westerveld et al.[32] have reported a synteny between 6-phosphogluconate dehydrogenase (PGD) and Pep C. Taken together, these findings imply that PGD, Pep C, and PGM$_1$ are all syntenic. Pep C has been assigned to chromosome 1 using mouse–human cell hybrids[31]. This assignment has been confirmed by the assignment of PGD to chromosome 1 independently by Bootsma et al. (personal communication) and Hamerton et al.[34] using Chinese hamster–human hybrids. If the findings based on cell hybrids are combined with linkages known from human pedigree analysis, the following additional gene markers can be assigned to chromosome 1: zonular pulverulent cataract, Duffy blood group, auriculoosteodysplasia, salivary amylase, pancreatic amylase, elliptocytosis and rhesus blood group. For complete literature citations see Ruddle et al.[31].

Table 2 Assignments of Genes to Chromosomes

Chromosome	1	PGM$_1$, 17190; PGD, 17220; Pep C, 17000
Chromosome	2	IDH, 14770; MOR, 15425
Chromosome	3	—
Chromosome	4–5	Adenine B$^+$, 10265
Chromosome	6	MOD, 15420; IPO-B, 14745
Chromosome	7	MPI, 15455; PK$_3$, 17905
Chromosome	8–9	—
Chromosome	10	GOT, 13825
Chromosome	11	LDH-A, 15000; Es-A$_4$, 13340; KA, 14875
Chromosome	12	LDH-B, 15010; Pep B, 16990; GlyA$^+$ (serinehydroxymethylase ?), 13845
Chromosome	13	—
Chromosome	14	NP, 16405
Chromosome	15	
Chromosome	16	APRT, 10260
Chromosome	17	TK, 18830
Chromosome	18	Pep A, 16980
Chromosome	19	GPI, 23575
Chromosome	20	ADA, 10270
Chromosome	21	IPO-A, 14744; AVP, 10745
Chromosome	22	—
Chromosome	X	HGPRT, 30800; PGK, 31180; GPD, 30590; α-Gal, 30150
Chromosome	Y	—

These genes were assigned or confirmed by cell hybrid analysis. Each trait is identified by McKusick's human gene catalogue number[59]. IPO-A and B used here agree with the original designation of Brewer[33].

Preliminary results in our laboratory (R. P. Creagan and F. H. R.) suggest that isocitrate dehydrogenase (IDH) and NADP-malate dehydrogenase (MOD) which have been shown to be syntenic[44] can be assigned to chromosome 2. No loci have been assigned to chromosome 3. For chromosomes 4 and 5, Kao and Puck[35] using Chinese hamster–human

hybrids have demonstrated a positive association between hamster adenine B auxotrophy and a human B group chromosome when hybrids are propagated on minimal medium The specific enzyme involved is unknown. Chen et al.[36] usging mouse–human hybrids have shown that cytoplasmic malate dehydrogenase (MOD) is assignable to chromosome 6 and there is evidence to support a synthetic relationship between indolephenol oxidase, tetrameric form B (IPO-B) and MOD (J. A. Tischfield, R. P. Creagan and F. H. R., unpublished).

McMorris et al.[37] using mouse X human hybrids have assigned mannose phosphate isomerase (MPI) to chromosome 7. Shows[38] has reported a syntenic relationship between MPI and the leucocytic form of pyruvate kinase$_3$ (PK$_3$).

There are no assignments to chromosomes 8 or 9. There is evidence from mouse–human hybrids for the assignment of the cytoplasmic form of glutamate oxaloacetate transaminase (GOT) to chromosome 10 (unpublished work of R. P. Creagan, J. A. Tischfield, F. A. McMorris, M. Hirschi, T. R. Chen and F. H. R.)

Boone et al.[29] using mouse–human hybrids have assigned lactate dehydrogenase A (LDH-A) to chromosome 11. Shows[39] using mouse–human hybrids has reported a syntenic association between LDH-A and human esterase A$_4$ (EsA$_4$). Van Someren et al.[40] have reported a syntenic association between glutamic-pyruvic transaminase (GPT-C) and LDH-A. The possibility exists, however, that their enzyme detection system is recording LDH-A activity. This may also apply to LDH-B and GPT-B (see below). Nabholz et al.[17] using mouse–human cells have reported a positive correlation between the segregation of LDH-A or B activity and sensitivity of hybrid cells to anti-human cytotoxic antisera. Puck et al.[41] have reported on the segregation of a possibly similar human antigen(s) in Chinese hamster–human hybrid cells, which they have found to be syntenic with LDH-A.

Ruddle and Chen[42] and Chen et al.[36] using mouse–human hybrids have demonstrated positive correlation between lactate dehydrogenase B (LDH-B) and chromosome 12. Hamerton et al.[34] have confirmed this assignment using Chinese hamster–human hybrids. In mouse–human hybrids a syntenic relationship has been demonstrated between LDH-B and peptidase-B (Pep-B)[14,43]. The Pep-B/LDH-B synteny has been confirmed by Shows[39,44], Van Cong et al.[30] and van Someren et al., who have also reported a syntenic association between glutamic-pyruvic transaminase-B (GPT-B) and LDH-B[40]. Jones et al.[15] using Chinese hamster–human hybrids have reported a syntenic relationship between LDH-B and the complement to the Chinese hamster glycine auxotrophic mutant A. Serine hydroxymethylase has been implicated as the specific deficiency in glycine A auxotrophy.

No assignments have been made to chromosome 13. For chromosome 14, Ricciuti and Ruddle (ref. 46 and F. Ricciuti and F. H. R., unpublished) using a 14/X translocation in a human diploid fibroblastic cell strain (KOP) hybridized to a mouse cell line have demonstrated a segregation of nucleoside phosphorylase (NP) with the X linked markers, HGPRT, GPD, and PGK. Somatic cell genetic[46] and family studies[47] have provided evidence for the autosomal linkage of NP. The studies of Ricciuti and Ruddle thereby support the assignment of NP to chromosome 14. Unreported experiments from our laboratory using a 14/22 translocation also confirm the assignment of NP to 14. Hamerton et al.[34] have reported results based on Chinese hamster–mouse hybrids which are consistent with the above findings of Ricciuti and Ruddle. No assignments have been made to chromosome 15.

Tischfield and Ruddle (unpublished) using an adenine phosphoribosyltransferase (APRT) deficient mouse cell line hybridized to normal human diploid cells have obtained evidence for the assignment of APRT to chromosome 16.

On evidence from family studies, Robson et al.[48] have assigned α-haptoglobin to chromosome 16. APRT activity variants have been reported in man, and it would be reasonable to identify kindreds in which α-haptoglobin and APRT variants are jointly expressed to test for linkage between these two markers.

For chromosome 17, Green[49] and Migeon and Miller[50] using mouse–human cell hybrids assigned thymidine kinase (TK) to an E group chromosome. This assignment was based on the earlier findings of Weiss and Green[4] and has since been verified by Boone and Ruddle[51]. Miller et al.[52], Ruddle and Chen[53], and Boone et al.[29] have now assigned TK specifically to chromosome 17. Boone et al.[29], making use of a spontaneously occurring 17 translocation to a mouse chromosome, have provided evidence for the assignment of TK to the long arm of chromosome 17. Kit et al.[54] and McDougall et al.[55] have demonstrated that adenovirus 12 infection induces host TK activity, and concurrently a secondary constriction in the proximal segment of the long arm of 17. These findings suggest that the TK gene may be located near the adeno-12 induced gap region.

Creagan et al. (unpublished) using mouse–human cell hybrids have provided evidence for the assignment of peptidase-A (Pep-A) to chromosome 18.

Glucosephosphate isomerase (GPI) has been assigned to chromosome 19 on the basis of evidence from mouse–human cell hybrids[37]. Hamerton et al.[34] have confirmed this assignment using Chinese hamster–human cell hybrids. Linkage studies in the mouse have revealed a loose linkage between GPI and β haemoglobin: it will be of interest to test for a similar linkage relationship in human kindreds.

Boone et al.[29] using mouse–human hybrids reported a weak association between cytoplasmic isocitrate dehydrogenase (IDH), cytoplasmic maleate oxidoreductase (MOR) and chromosome 20. More extensive data from mouse–human hybrids have now shown that IDH and MOR cannot be assigned to 20 and using mouse–human hybrids we have obtained evidence of the assignment of tissue-specific adenosine deaminase (ADA) to chromosome 20 (J. A. Tischfield, R. P. Creagan and F. H. R., unpublished). ADA is asyntenic with both IDH and MOR. Family studies have demonstrated linkage between HL-A phosphoglucomutase 3, P blood group, and ADA[56].

On chromosome 21, Tan et al.[57], using somatic cell hybrids, have provided evidence for the syntenic association between indolephenoloxidase-A, dimeric (IPO-A) and a genetic factor (AVP) which controls an antiviral response specifically induced by human interferon. The genetic factor may regulate the interferon receptor and/or the antiviral protein. We have also shown that the interferon and AVP loci are asyntenic[57]. These results confirm earlier studies by Cassingena et al.[58] on their asyntenic association based on monkey–rat somatic cell hybrids. Tan et al.[57] have assigned AVP/IPO-A to chromosome 21. No assignments have yet been made to chromosome 22.

Glucose-6-phosphate dehydrogenase (GPD), hypoxanthine-guanine phosphoribosyltransferase (HGPRT), and phosphoglycerate kinase (PGK) have all been assigned to the X chromosome by segregation analysis in families[59]. Nabholz et al.[17] using mouse–human hybrids confirmed the X linkage of HGPRT. Meera Kahn et al.[60] have demonstrated the X linkage of PGK by cell hybrid analysis. Ruddle et al.[61] using mouse–human hybrids confirmed the X linkage of HGPRT, glucose-6-phosphate dehydrogenase (GPD), and phosphoglycerate kinase (PGK). Grzeschik et al.[62] have recently provided evidence based on Chinese hamster–human hybrids for the assignment of α-galactosidase (α-Gal) to the X chromosome. In an earlier report, Grzeschik et al.[63] analysed cell hybrids between human KOP cells which possess a 14/X translocation (KOP) and mouse and Syrian hamster cells. They observed an infrequent segregation of HGPRT and GPD from PGK, which led

them to postulate the assignment of PGK to the long arm, and the possible assignment of HGPRT and GPD to the short arm, although assignment to the long arm was not altogether discounted. Ricciuti and Ruddle (ref. 46 and unpublished results) using the same KOP material hybridized to mouse cells have obtained data which indicate that all three markers are located on the X long arm. This suggests that PGK is proximal to the centromere and distant from the other two markers. HGPRT and GPD seem to be close together and distal to the centromere with respect to PGK; preliminary evidence indicates that HGPRT is proximal to GPD. P. Gerald and co-workers (personal communication) have recently studied a human cell with a 19/X translocation hybridized to mouse cells. A translocation product composed of the 19 long arm, the proximal half of 19 short arm, and the distal half of the X long arm was correlated with GPI, HGPRT, and GPD, but not PGK. This result is consistent with the human X linkage map proposed by Ricciuti and Ruddle[46]. It also confirms the assignment of GPI to 19.

No assignments have been made to the Y chromosome.

Possibilities for New Approaches

The development of a detailed human genetic map is certain to provide insight into the evolutionary origins of man and the primates. LDH-A and LDH-B are located on chromosomes 11 and 12 respectively. These chromosomes are similar in size, centromere position, and banding pattern, which is consistent with the occurrence of a primordial polyploid event in the early primate genome as discussed by Comings[64]. Somatic cell genetic analysis should be feasible for representative members of the order primates using rodent–primate hybrids. Linkage data from such hybrids should provide information on the relatedness of these forms, and yield estimates for rates of evolutionary divergence, especially when combined with comparative studies on the chromosome constitutions and amino-acid sequences of proteins in the representative specimens.

It is already obvious that somatic cell genetics has contributed and will in the future contribute important data to human genetics. Moreover, these developments enhance the significance and future role of family and population genetic studies. Already map distances between genes have been refined or established by the certain knowledge from somatic cell genetics that certain gene pairs are syntenic. We should expect a fruitful interaction and collaboration between practitioners of somatic cell genetics and classical genetics. We must, however, keep clearly in mind that somatic genetic procedures as they now exist are still unacceptably slow and linkage estimates cannot yet be made. If we are soon to develop genetic maps of man comparable to those available for the lower eukaryotes, it will be necessary to develop new procedures. Possibilities for this are to be found in somatic cell recombination and gene transfer.

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Further Evidence of Lower Pleistocene Hominids from East Rudolf, North Kenya, 1972

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Thirty-eight fossil hominids were collected during the 1972 season at East Rudolf, and the total now known from this locality is eighty-seven. Several specimens, including some attributable to *Homo*, were recovered from deposits that are below the KBS Tuff dated at 2.61 million years.

THIS report summarizes the results of the continuation of work carried out during 1972 at East Rudolf. Preliminary reports for the years 1968–1971 have already been published[1-3].

A further thirty-eight fossil hominids were collected during 1972, bringing the total now known from this locality to eighty-seven. The collection includes cranial and postcranial material. Several specimens were recovered from deposits that are below the KBS Tuff (2.61 m.y.[4]); these are of particular interest in view of the presence of at least two distinct forms of hominid at this early period. In this report, as before[1-3], I have avoided specific identifications and have made provisional attributions to either *Australopithecus* or *Homo*. I believe that the final analysis of the hominids from East Rudolf should be based on as large a sample as can be reasonably available, and there is every indication that further material will be recovered with the continued investigation of the area.

The palaeontological investigations were directed by Dr J. M. Harris (Kenya National Museums), and further specimens of several taxa were collected. Some specimens collected from below the KBS Tuff should prove of considerable interest and value regarding the interpretation of the lower Pleistocene genera[5]. With the extension of exploration at East Rudolf, a unified system of locality numbers designating collecting areas has been devised by Dr V. Maglio who has provided an area map and a simplified diagrammatic representation of correlations between the principal areas[5].

Archaeological exploration and excavations were continued under the supervision of Professor Glynn Isaac (University of California, Berkeley), assisted by graduate students. The excavations within the KBS Tuff[6] were extended and a series of sites above the KBS Tuff were examined; a large collection of artefacts was recovered from several preliminary excavations. A detailed report on the archaeological activities will be presented elsewhere.

Mr Bruce Bowen (Iowa State University) extended the geological survey and mapping south of the Koobi Fora ridge

and has established the broad continuity of the sequence from the lowest deposits at Kubi Algi, about 4.5 m.y., to the uppermost deposits at Ileret, about 1.0 m.y.

Mr Ian Findlater (Birkbeck College, London) continued the field investigation and mapping of volcanic events, and Drs J. Miller and F. Fitch are dating the volcanic horizons. In spite of meticulous collecting and rigorous laboratory analysis, however, dates for the tuffaceous horizons above the KBS Tuff continue to prove unreliable. Some intriguing technical problems indicate that depositional complications are causing the conventional techniques of radiometric age determinations to give inconclusive results. Thus there has been no advance on the situation as reported by Maglio[5], although there is no evidence to suggest that the 2.61 ± 0.26 m.y. BP date from the KBS Tuff is unreliable (personal communication from J. A. Miller). The continued palaeomagnetic studies by Dr A. Brock (University of Nairobi) together with faunal correlations further strengthen confidence in this date.
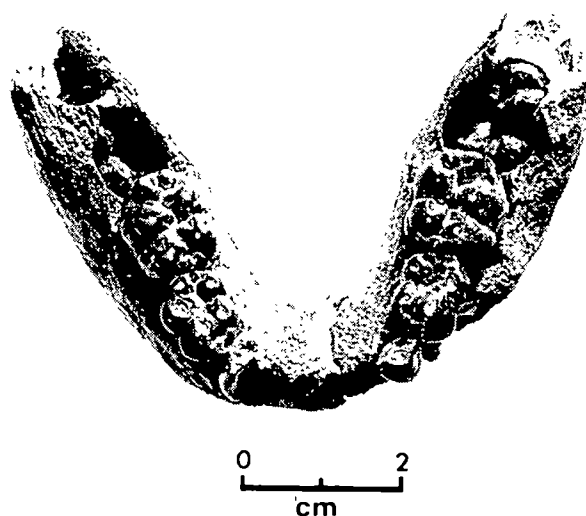
Fig. 1 Occlusal view of juvenile mandible KNM-ER 1477.

In the summary which follows of the 1972 hominid collection a brief mention is made of the more important specimens; detailed descriptions of all the specimens will be given shortly elsewhere. The specimens attributed to *Australopithecus* are

listed in Table 1; the specimens attributed to *Homo* are listed in Table 2; and the specimens which have not yet been attributed to a particular genus, either because they are too fragmentary, or because a more detailed study is first required, are listed in Table 3. These tables also include geographical and stratigraphical data. The stratigraphical correlation of the areas 119, 121, 123, 127 south of the Koobi Fora ridge has yet to be concluded, so, for the present, this information is omitted for specimens from these areas. Specimens 1510 and 1590 to 1593 were discovered after the 1972 expedition had closed its principal research activities; these specimens, although important, are therefore only listed in the tables and not mentioned further. A separate article will be published[7] giving details of the *Homo* specimens, KNM-ER 1470, 1472, 1475 and 1481, in order to allow adequate treatment of these important finds.

Australopithecine Material

Eighteen individuals, listed in Table 1, were collected. A number of specimens represent associated parts from the same individual. Several finds refer to horizons below the KBS Tuff so that there is now evidence of the species at East Rudolf during a period of more than 1 m.y.

Table 1 1972 Material Attributed to *Australopithecus*

KNM-ER No.	Specimen detail	Area	Stratigraphic position where known
1463	Right femur diaphysis	1A	Below middle tuff
1464	Right talus	6	Below lower tuff
1465	Proximal fragment left femur	8	Below upper tuff
1467	Isolated M_3	3	Below upper tuff
1468	Right mandible	8	Below middle tuff
1469	Left mandible, M_3	131	Below KBS Tuff
1471	Proximal half right tibia	131	Below KBS Tuff
1476	Left talus, proximal tibia and fragment tibia shaft	105	At or above KBS Tuff
1477	Juvenile mandible with teeth	105	At or above KBS Tuff
1478	Cranial fragments	105	At or above KBS Tuff
1479	Fragments isolated molars	105	At or above KBS Tuff
1500	Skeletal elements	130	Below KBS Tuff
1503	Proximal right femur	123	—
1504	Distal right humerus	123	—
1505	Proximal fragment left femur and fragment of shaft	123	—
1506	Right mandible, M_1, M_2 and isolated P^4, P^3		—
1509	Isolated teeth, P_4–M_3	119	—
1592	Distal half femur	12	Below lower tuff

A left half of a mandible, KNM-ER 1469, provides evidence that the large form of *Australopithecus* had developed before deposition of the KBS Tuff 2.6 m.y. ago. The mandible is cracked, although a large portion of M_3 is preserved *in situ* together with the roots and parts of the crowns of M_2 and M_1.

A mandibular fragment, KNM-ER 1506, includes M_1 and M_2 *in situ* and isolated P^3, P^4; the M_2 shows a distinct wear facet for M_3 but this tooth seems to have been lost before fossilization. The significance of the specimen is its small size; the body demonstrates the high degree of robusticity seen in other australopithecine mandibles from East Rudolf, and, for the first time, teeth of a small individual are preserved and provide crown dimensions.

A juvenile mandible, KNM-ER 1477 (see Fig. 1), discovered by Mr Musa Mbithi, a Kenyan, is beautifully preserved. The following teeth are in place: the left c, the left and right dm_1, dm_2 and erupting M_1. The germs of the left P_3 C, and I_2 were dislodged from their crypts and were recovered separately,
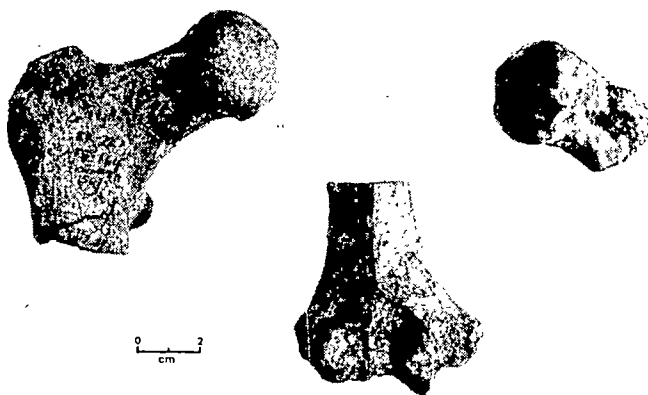
Fig. 2 Anterior views of (from left to right) femur KNM-ER 1503; humerus KNM-ER 1504; and femur KNM-ER 1505.

whereas the corresponding tooth germs on the right side are preserved within their crypts.

Several postcranial specimens were recovered and a significant difference in the size of some of the specimens may provide additional evidence of sexual dimorphism in this group[2,3]. A specimen, KNM-ER 1500, which was also recovered from deposits below the KBS Tuff, includes parts of an associated skeleton. The specimen—a small individual, probably female—was discovered by a Kenyan, Mr John Kimengech, and it represents the first certain association of upper and lower limb elements of *Australopithecus* from East Africa. Unfortunately the material is badly weathered and considerable detail has been lost. The following skeletal elements have been identified: the proximal portions of the right femur, radius and ulna, and left tibia; the distal portions of the right femur, and fibula and left tibia; and scraps of the shafts of the tibia, ulna and humerus. This specimen should provide important new evidence on limb proportions in addition to morphological details of australopithecine postcranial bones that have not been available before.

A specimen, KNM-ER 1476, provides information on an associated tibia and talus, the former showing features similar to the australopithecine tibia, KNM-ER 741[2,8], previously reported. The talus exhibits a marked lateral extension for the articulation of the lateral malleolus which is also seen in a complete talus, KNM-ER 1464. This feature seems to be a characteristic of australopithecine tali and together with a number of other features makes this foot bone quite distinctive of this group.

Three specimens collected from area 123, KNM-ER 1503, 1504 and 1505 (see Fig. 2), probably represent parts of the same individual. The proximal portion of the right femur, KNM-ER 1505, is beautifully preserved and shows the characteristic long neck and small head seen in all other australopithecine femora[9]. The distal fragment of humerus is very similar to the humerus, KNM-ER 739[2,8], but it is smaller. It shows the marked extension of the medial epicondyle, the constricted trochlea, and the relatively large capitulum.

Hominine Material

Sixteen individuals, listed in Table 2, are represented by the material collected during 1972. Evidence of *Homo* at levels below the 2.6 m.y. KBS Tuff horizon will be put forward on the basis of some remarkable material that will be discussed in a separate report[7].

A fragment of parietal, KNM-ER 1466, is notable; it is thick boned and bears a marked temporal ridge, features which are reminiscent of the calvaria from Olduvai Gorge (OH9)[10]. The specimen is unfortunately incomplete, and therefore cannot provide any conclusive evidence for the presence of this species at East Rudolf.
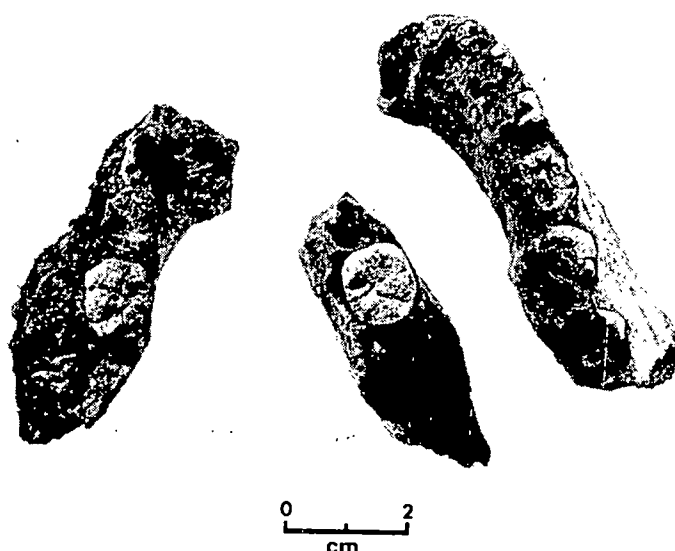
Fig. 3 Occlusal view of mandibles (from left to right) KNM-ER 1507, 1502 and 1501.

The mandibular fragments, KNM-ER 1501, 1502 and 1507 (see Fig. 3), from areas south of the Koobi Fora ridge are gracile and show a morphology similar to that seen on the *Homo* mandible from Ileret, KNM-ER 992[3].

Material of Unclear Affinities

Among the specimens listed in Table 3 a mandible, KNM-ER 1482 (see Fig. 4), is of particular interest; it shows characters not seen in either the contemporary *Australopithecus* or the assemblage of *Homo* mandibles from East Rudolf. The specimen was recovered from deposits below the KBS Tuff.

Significance of the 1972 Finds

The recovery of *Australopithecus* from levels below the KBS Tuff is particularly important in view of the close similarity of this material to that from the upper part of the East Rudolf succession. A pre-Pleistocene emergence of this genus seems reasonable although no precise data to support this have yet been put forward. Now that a large number of specimens to

Table 2 1972 Material Attributed to *Homo*

KNM-ER No.	Specimen detail	Area	Stratigraphic position where known
1462	Isolated M_3	130	Below KBS Tuff
1466	Parietal fragment	1	Below upper Tuff
1470	Cranium	131	Below KBS Tuff
1472	Right femur	131	Below KBS Tuff
1475	Proximal right femur	131	Below KBS Tuff
1480	Isolated molar	105	Above KBS Tuff
1481	Left femur, proximal tibia, distal tibia and distal fibula	131	Below KBS Tuff
1483	Mandible fragments	131	Below KBS Tuff
1501	Right mandible	123	—
1502	Right mandible with molar	123	—
1507	Juvenile left mandible with teeth	127	—
1508	Isolated molar	127	—
1510	Cranial fragments	119	—
1590	Cranial fragments with juvenile dentition	12	Below KBS Tuff
1591	Humerus lacking head	12	Above KBS Tuff
1593	Cranial and mandibular fragments	12	Below KBS Tuff

Table 3 1972 Material of Unclear Affinities

KNM-ER No.	Specimen detail	Area	Stratigraphic position where known
1473	Proximal fragment of right humerus	131	Below KBS Tuff
1474	Parietal fragment	131	Below KBS Tuff
1482	Mandible, partial dentition	131	Below KBS Tuff
1515	Isolated incisor	103	Below Koobi Fora Tuff

Australopithecus are known from East Africa, the taxonomic attribution of the mandibular specimen, KNM-ER 329 from Lothagam Hill, to *Australopithecus c.f. africanus*[11] might be questioned. The evidence for the presence of the "gracile" form of *Australopithecus* in East Africa is limited. The fragmentary nature of this specimen makes specific identification very difficult, particularly in the absence of other material from deposits of an equivalent age; only a few isolated dental fragments from the Usno Formation in the Omo Valley[12] are known. The generic attribution of the Lothagam specimen to *Australopithecus* might be questioned on the grounds that the specimen could equally well represent a Pliocene form such as the East African representative of the genus *Ramapithecus*. Such a conclusion would radically alter the interpretative model of hominid evolution.

The additional postcranial material will provide further evidence on which to examine the significance of the locomotory behaviour of *Australopithecus*. Although there is a growing body of evidence in support of a bipedal model, it is important to recognize that the australopithecine mode of bipedality may have been quite distinctive from that of other contemporary hominids and behaviourally significant. In view of the evidence for contemporary *Homo* with morphologically distinct limb elements, some consideration must be given as to whether the australopithecine pattern of bipedal adaptation really reflects a transitional phase as has been suggested. The associated skeletal material collected during 1972 will advance the study of limb proportions within *Australopithecus*; preliminary indications point to a relatively short lower limb and a longer forelimb.

Fig. 4 Occlusal view of mandible KNM-ER 1482.

The hominine collection provides further examples of the gracile mandibles previously reported from the Ileret area[3]. Although the dating for the deposits south of Koobi Fora remains tentative, the fauna associated with these new mandibles indicates that they are earlier than those from Ileret. As such, it is possible to postulate a range of time that is greater than that represented by Ileret and the Olduvai Bed II deposits from which similar material has been reported. Mandibular material for the hominid represented by the cranium, KNM-ER 1470[7], is not known at present but the size and shape of the palate of this specimen suggest a fairly broad big-toothed mandible, quite unlike the gracile specimens just mentioned. The affinities of the mandible, KNM-ER 1482, found in the same locality as the cranium KNM-ER 1470, are far from clear.

In conclusion, I would like to stress that the 1972 collection of hominids has raised more questions than answers; it now seems clear that the pattern of hominid evolution in eastern Africa is extremely complex. Evidence for local geographical variation in various mammalian taxa, primate and non-primate, is emerging, with significant differences occurring within forms restricted to small geographical zones such as the Omo/East Rudolf basin. Until further data on palaeogeographical barriers, environments and chronology are available the interpretation and the erection of evolutionary models should remain tentative.

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Particle Injection in the Cygnus X-3 Radio Outburst

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Particle injection played an important role in the recent Cygnus X-3 radio outburst. Calculations on the basis of an improved expanding cloud model show that a maximum mass of $0.76 \times 10^{-8} \, M_\odot$ was injected over a period of 1.2 days.

THE mass of data from the recent radio outbursts in Cygnus X-3 provides an excellent opportunity to test ideas on radio variability. Monitored at least at eight frequencies during its entire ten day duration, the first of these outbursts yielded flux density data complete and well-defined enough to allow more precise determination of model parameters than previously possible for events of this kind. Here I examine in detail the first of these outbursts (September 2–11) using the generally accepted adiabatic expansion model modified to incorporate a prolonged injection.

According to the conventional model, the observed flux is synchrotron radiation produced by an adiabatically expanding cloud of relativistic electrons. Initially, the cloud is small and the electron density high enough for re-absorption of the synchrotron radiation to occur; the cloud is opaque to its own radiation. As the cloud expands, the decreasing electron density results in an increase in the observed flux at a given frequency. The flux density reaches a peak just as the cloud makes the transition from its opaque to its transparent phase where the electron density is low enough for re-absorption to be negligible. At the higher frequencies, the flux density peaks earlier since the more energetic radiation penetrates the cloud more readily. Finally, the flux falls off as the electrons continue to lose energy to the adiabatic expansion. In this formulation of the model, the number of electrons is assumed to be constant throughout source evolution.

This model accounts well for the flux density development during the late part of the outburst[1], but fails by a wide margin to fit the development at the beginning. The problem is highlighted in the discrepancy between the peak flux densities observed at the high frequencies, and the much higher values required by the model. The origin of this discrepancy lies with the model assumption that all electrons are present and radiating in the source from the beginning. According to the model, the source should become quickly transparent at the high frequencies and yield high fluxes before expansion losses significantly reduce electron energy. Only if fewer relativistic electrons are present initially in the source or if some additional suppression mechanism other than self-absorption is at work can the adiabatic expansion model be made to conform with the data.

The simple device of a particle injection of specific duration,

which can be expressed analytically in the model equations, significantly improves the model's description of the Cygnus X-3 outburst. If electrons are introduced gradually into the source so that there are a small number initially producing a correspondingly small flux which builds as the electron number increases, then the observed behaviour of the flux density may be adequately reproduced.

Model Equations

I adopt a rate of particle injection which is constant over a time ζ, after which it falls to zero. It may be represented by the normalized form:

$$dN/dt = (1 + \exp(t - \zeta)/\varepsilon)^{-1} \underset{\varepsilon \ll t - \zeta}{\simeq} \begin{cases} 1; & t < \zeta \\ 0; & t > \zeta \end{cases} \quad (1)$$

N is the total number of electrons injected into the source as a function of time; ε is the time scale for the injection rate to fall to zero. For small ε, the rate is simply a step function. This is not the only allowed form for the injection rate. Its simplicity and previous success at interpreting similar outbursts in extragalactic radio sources[2] recommend its further application here.

The flux density observed from a self-absorbed spherical cloud composed of synchrotron radiating electrons isotropic in velocity and uniform in spatial distribution is[3,4]

$$S_\nu = \pi a_\gamma (3.18 \times 10^{-31}) r^2 R^{-2} H^{-1/2} \nu^{2.5} [1 - e^{-\tau}] \quad (2a)$$

$$\tau = 2b_\gamma (0.019)(3.5 \times 10^9)^\gamma rKH^{(\gamma+2)/2} \nu^{-(\gamma+4)/2} \quad (2b)$$

where τ is the source opacity. The frequency of observed radiation ν, the magnetic field strength in the source H, the distance, R, to the source, and its radius r, must be given in c.g.s. units. The coefficients a_γ and b_γ are known, slowly varying functions of γ of order unity. The factors π and 2 derive from the geometry of the source. K and γ occur in the electron differential energy distribution, which is assumed to be a power law:

$$n(E, t)\, dE = KE^{-\gamma}\, dE \quad (3)$$

n represents the number of electrons per unit volume in the energy interval E to $E + dE$. From equations (1) and (3) with the fundamental assumption that the electrons lose energy as r^{-1} to the adiabatic expansion, it follows that K must have the form:

$$K = k(r/r_0)^{-2-\gamma} f(t) \quad (4a)$$

$$f(t) = \varepsilon \ln(1 + \exp(\zeta/\varepsilon))(1 + \exp(-(t-\zeta)/\varepsilon)^{-1}$$
$$\underset{\varepsilon \ll t - \zeta}{\simeq} \begin{cases} t; & t < \zeta \\ \zeta; & t > \zeta \end{cases} \quad (4b)$$

where k is a constant, and r_0 is the initial source size. The effect of the injection shows up at times earlier than ζ; after $t = \zeta$, the injection rate falls to zero, and $K \propto r^{-2-\gamma}$, the dependence occurring in the conventional formulation of the model. If the transition time ε is small compared with the difference $t - \zeta$, then the indicated approximation may be used.

To make the time dependence in equation (2) explicit, I let $r = r_0 + Vt$ where V is the constant expansion velocity. Then, because the adiabatic nature of the expansion implies that $H \propto r^{-2}$,

$$S_\nu = a(t + \rho)^3 \nu^{2.5} [1 - e^{-\tau}] \quad (5a)$$

$$\tau = b(t + \rho)^{-2\gamma-3} \nu^{-(\gamma+4)/2} f(t) \quad (5b)$$

where $\rho = r_0/V$, and

$$a = a_\gamma (10^{-30}) (r_0/R)^2 H_0^{-1/2} \rho^{-3} (10^9)^{2.5} 10^{23} \quad (6)$$

$$b = b_\gamma (0.038)(3.5 \times 10^9)^\gamma r_0 k H_0^{(\gamma+2)/2} \rho^{2\gamma+3} (10^9)^{-(\gamma+4)/2} \quad (7)$$

Equation (5) is in convenient form for least squares fitting. The coefficients a and b are adjusted so that in equation (5) the frequency must be in GHz and the flux density in f.u. The time, t, is actually the difference $t' - t_0$, where t' is the time of observation and t_0 is the initial time. t_0 is interpreted as the time when the model becomes applicable. t and ρ must have the same units of time, in this case days.

Fit to the Data

The results of model fitting to the data at 2.7 and 8.085 GHz (ref. 5) are presented here. Having been taken simultaneously, the flux density readings at these two frequencies do not raise the difficulty of coordinating data at several frequencies at differing times in the equations. Least squares fitting of equation (5) for the parameters ζ, ρ, a, and b for a matrix of values for γ and t_0 leads to the following results:

$$\gamma = 1.7$$
$$t_0 = 0.4 \text{ (September 2, 0930 UT)}$$
$$\zeta = 1.16 \text{ (September 3, 1430 UT)}$$
$$\rho = 1.85$$
$$a = 0.068$$
$$b = 2.1 \times 10^4$$

The root mean square deviation calculated for this fit was 0.65 f.u. γ and t_0 were varied in steps of 0.05 in arriving at these values. $\gamma = 1.7$ corresponds to a spectral index of $\alpha = -0.35$ for a transparent synchrotron source with a power-law spectrum $S \propto \nu^\alpha$. The initial time, t_0, is 0.4 day past 0 h UT, September 2, which was taken as a convenient reference time. The injection time, ζ, shows that particles were being injected into the source for more than a day after t_0. For the initial development of the source, injection is an important process.

The parameter ε does not appear in the above list of least squares determined parameters because it drops from the equations in the quick transition approximation of equation (4). The validity of this approximation is supported in the improved root mean square generated by successively smaller ε values employed in making fits using the exact expression; smaller values for ε improved the least squares fit by giving slightly smaller root mean square values down to the limits set on the exponential routine by the computer. If the selected form for the injection rate is correct, then the discontinuous transition from a constant injection to zero, and not a slow fall off in the injection rate, must be considered in interpreting the origin of the injection.

In Fig. 1 I display the data points at 8.085 and 2.7 GHz as well as the least squares determined flux density curves. The model's easy reproduction of the observed peak value in the flux density at the high frequency confirms the importance of a prolonged injection. A plot of the opacity, equation (5b), with the least squares determined parameters (Fig. 2), shows the behaviour of the self-absorption process in the source. At the low frequency, the opacity remains just greater than one until the flux density peaks; the source is initially weakly self-absorbed at this frequency. At the higher frequency, the opacity never exceeds unity; the density of electrons never got high enough to cause self-absorption at this frequency. The effect of internal structure, which is most likely due to inhomogeneities in the magnetic field, shows up at the high

frequency because the source was always transparent there: at least two peaks may be made out in the 8.085 GHz flux density data before the injection ends. This additional variation does not appear in the flux density data at the low frequency.

A still more impressive result confirming the importance of injection is the comparison of observed time and value of the flux density maxima at the various frequencies of observation, with the model predictions on the basis of the least squares fit to the data at 2.7 and 8.085 GHz just presented. Table 1 lists these observed and predicted maximum flux density values for 7 frequencies. The more rapid variations in flux at the high frequencies are especially clear at 10.5 and 8.085 GHz; for these two frequencies, maximum flux density values for each of two discernible peaks are given with the corresponding times of maxima. At 15.5 and, 6.6 GHz, the other two frequencies for which the source was always transparent, this fine structure does not appear in the data because observations began late at these frequencies. The model does not reproduce the fine structure; it averages over these variations to arrive at a single peak flux density for each frequency. But the agreement of the model with the general behaviour of the data, especially at the high frequencies where the conventional model falls apart, is clear.

Fig. 2 Synchrotron self-absorption opacity corresponding to the flux density curves in Fig. 1.

Table 1 Observed and Theoretical Values for Flux Density Maxima and Times of Maxima for Seven Frequencies of Observation

Frequency (GHz)	Observed S_{max} (f.u.)	Observed t_{max} * (day)	Theoretical S_{max} (f.u.)	Theoretical t_{max} * (day)
15.5	16.6	1.22	16.0	1.18
10.5	22.7 (17) 20.9	0.98, 1.23	18.1	1.19
8.085	20.4 (19) 20.2	1.21, 1.32	19.4	1.21
6.6	≥ 22.0	≤ 1.31	20.2	1.25
2.7	16.0	1.5	15.8	1.56
1.68	7.2	2.3	9.1	2.2
0.41	2.0	5.25	1.8	5.4

* Measured from 0 h UT, September 2.

The theoretical values are those predicted from a least squares fit to the data at 8.085 and 2.7 GHz. Observed S_{max} and t_{max} values are taken from ref. 8 (15.5 GHz), ref. 9 (10.5, 6.6 GHz), ref. 5 (8.085, 2.7 GHz), ref. 10 (1.68 GHz),.and ref. 11 (0.41 GHz). Corresponding to the double peaks in flux discerned at 10.5 and 8.085 GHz, two values each for observed S_{max} and t_{max} are listed; the numbers in parentheses indicate the minimum between peaks. The low flux maximum reported at 1.68 GHz is most probably the result of subtracting out too high a base level.

Fig. 1 Cygnus X-3 flux density data and least squares fitted curves at 8.085 (×) and 2.7 (●) GHz.. The data were taken from ref. 5.

Physical Conditions of the Cloud; Mass Injection Rate

The parameters ρ, a and b determined in the least squares fit give information about the physical makeup of the expanding cloud. For example, from equation (6), the initial field H_0 may be calculated:

$$H_0 = (10^{-30} a_\gamma/a)^2 (r_0/R)^4 \rho^{-6} (10^{91})$$
$$= 8.2 \times 10^{31} (r_0/R)^4 \tag{8}$$

where $a_\gamma = 1.22$ for $\gamma = 1.7$. Specification of the initial cloud radius, r_0, and the distance to the cloud, R, gives H_0. Although one estimate[6] put the source between 8 and 11 kpc, no hard data on the source size were collected. Model consistency arguments must be used to set limits on r_0 so that source conditions may be determined.

A lower limit on r_0 follows from the requirement that the

plasma associated with the injected relativistic electrons be rarefied enough to be transparent to the synchrotron radiation generated in the cloud. If the plasma has electron density n_{pl} and magnetic field H, then frequencies ν_0, of synchrotron radiation for which

$$\nu_0 > 20 \ n_{pl}/H \tag{9}$$

are observable[4]. This limitation merely backs up the assumption that self-absorption by the relativistic electrons is the only mechanism which renders the cloud opaque to its own radiation. Other limitations on the plasma density (for example, thermal opacity, brehmsstrahlung losses) are, it turns out, not as stringent.

The density of relativistic electrons injected into the cloud is determined by integrating equation (3) over energy between the cutoff energies E_1 and E_2, the energies of the highest and lowest energy electrons in the cloud:

$$n(t) = \int_{E_1}^{E_2} n(E,t) dE = K(E_2^{1-\gamma} - E_1^{1-\gamma})/(1 - \gamma) \tag{10}$$

Because for each electron energy $E = E_0(r_0/r)$, and because an electron of initial energy, E_0, radiates most strongly at frequency $\nu = 6.27 \times 10^{18} \ H_0 E_0^2$ Hz,

Table 2 Values for Several Source Properties for Five Assumed Initial Source Radii

r_0	1.5×10^{14}	2×10^{14}	2.5×10^{14}	3×10^{14}	3.5×10^{14}
Magnetic field strength	0.017	0.054	0.13	0.28	0.51
Relativistic electron density	1.7×10^5	2.3×10^4	4.8×10^3	1.4×10^3	460
Energy in magnetic field	7.2×10^{38}	1.7×10^{40}	2×10^{41}	1.4×10^3	8×10^{42}
Energy in relativistic electrons	3.3×10^{44}	5.9×10^{43}	1.6×10^{43}	1.5×10^{42}	2.1×10^{42}
Expansion velocity	$0.031c$	$0.042c$	$0.052c$	$0.063c$	$0.073c$

With the exception of those for the initial radius, r_0, and the constant expansion velocity which applies throughout source evolution, the values correspond to possible descriptions of the source at 1.2 day into source evolution, when particle injection ends. All quantities are in c.g.s. units except where otherwise indicated.

$$n(t) = K(\nu_1/(6.27 \times 10^{18} H_0))^{(1-\gamma)/2} (r/r_0)^{\gamma-1}$$

where $F_\nu = ((\nu_2/\nu_1)^{(1-\gamma)/2} - 1)/(1-\gamma)$ (11)

The density of relativistic electrons maximizes near $t = \zeta$, when all the electrons have been injected into the source:

$$n(\zeta) = k(\zeta)(\nu_1/6.27 \times 10^{18} H_0))^{(1-\gamma)/2}(1+\zeta/\rho)^{\gamma-1} F_\nu \quad (12)$$

The maximum allowable plasma electron density consistent with equation (9) occurs when $n_{pl} = n(\zeta)$. Thus, from equations (9) and (12), the condition which gives the minimum source radius is

$$\nu_0 H/20 > k(\zeta)(\nu_1/(6.27 \times 10^{18} H_0))^{(1-\gamma)/2}(1+\zeta/\rho)^{\gamma-1} F_\nu \quad (13)$$

The expression defining the lower limit on r_0 results on substituting from equations (4), (6) and (7):

$$r_0^{11} > \left(\frac{a}{1.22 \times 10^{-30}}\right)^5 \left(\frac{b}{3.22 \times 10^{14}}\right)$$
$$\rho^{-2\gamma+12}(10^9)^{(\gamma-21)/2}(10^{23})^{-5}$$
$$\times \left(\frac{20}{\nu_0}\right)\left(\frac{\nu_1}{6.27 \times 10^{18}}\right)^{\frac{1-\gamma}{2}}\left(\frac{\zeta}{\rho+\zeta}\right) R^{10} F_\nu \quad (14)$$

where $b_\gamma = 0.506$ for $\gamma = 1.7$ has been used. Values for ν_1, ν_2, ν_0 and R must be chosen, the least squares fitted parameters having already been determined. The large power on r_0 makes it practically insensitive to choice of ν_1, ν_2 and ν_0. I let $\nu_1 = 10^7$ Hz and $\nu_2 = 10^{11}$ Hz, corresponding to wavelengths in the radio range. The lowest frequency at which the source was observed was 0.4 GHz; I set $\nu_0 = 10^8$ Hz. For $R = 10$ kpc, the lower limit on the source radius must be: $r_0 > 1.6 \times 10^{14}$ cm.

An upper limit on r_0 follows from the condition that there be more energy in the relativistic electrons than in the magnetic field so that the field does not confine the electrons:

$$u_e > H^2/8\pi \quad (15)$$

where u_e represents the energy density in the relativistic electrons. A second lengthy derivation beginning with the determination of u_e from equation (3), leads to the result

$$r_0^{17} < \left(\frac{a}{1.22 \times 10^{-30}}\right)^8 \left(\frac{b}{3.22 \times 10^{14}}\right) \rho^{-2\gamma+21}(10^9)^{(\gamma-36)/2}$$
$$\times (10^{23})^{-8} \zeta \left(\frac{\nu_2}{6.27 \times 10^{18}}\right)^{\frac{2-\gamma}{2}} R^{16} \left[\frac{1 - \left(\frac{\nu_1}{\nu_2}\right)^{\frac{2-\gamma}{2}}}{2-\gamma}\right] \quad (16)$$

Again, for $R = 10$ kpc, and ν_1 and ν_2 equal 10^7 and 10^{11} Hz respectively, the upper limit is $r_0 < 3.2 \times 10^{14}$. This maximum radius is smaller by more than an order of magnitude than the maximum set by the time scale for the flux variation.

With these limits on r_0, it is possible to fill out the description of the cloud. Equation (8) leads to the following limiting values for the initial magnetic field (in gauss):

$$0.062 < H_0 < 0.97$$

The number of electrons injected into the cloud is calculated from equation (12) with appropriate substitutions:

$$N = \frac{4}{3} \pi \left(\frac{a}{1.22 \times 10^{-30}}\right)^3 \left(\frac{b}{3.22 \times 10^{14}}\right) \rho^{-2\gamma+6}(10^9)^{(\gamma-11)/2}$$
$$\times (10^{23})^{-3} \zeta F_\nu r_0^{-4} R^6 \left(\frac{\nu_1}{6.27 \times 10^{18}}\right)^{\frac{1-\gamma}{2}} \quad (17)$$

For the usual values of R, ν_1 and ν_2, the maximum number of injected electrons (corresponding to $r_0 = 1.6 \times 10^{14}$ cm) is: $N = 8.9 \times 10^{48}$. For this situation, for which r_0 is minimum, the maximum electron number is also the maximum number of protons in the accompanying plasma, so we also have an upper limit on the mass of the injected cloud: $M < 0.76 \times 10^{-8} M_\odot$. Thus, the maximum possible rate at which mass was injected into the cloud, according to this model, is

$$\frac{dN}{dt} < 0.65 \times 10^{-8} M_\odot \text{ day}^{-1}; \quad t < 1.16 \text{ day}$$

These calculations are summarized in Table 2 with derived values for other source properties. The expansion velocity listed in the table is determined from the parameter $\rho = r_0/V$. Because it is only a small fraction of the light speed, c, the tabulated source properties require no correction for relativistic expansion.

Another Possible Absorption Mechanism

A development which the model is unable to reproduce is the observed evolution of the spectral index α. Both the observations and the model curves show that the source became transparent at the lower self-absorbed frequency when the flux maximized at that frequency. For a transparent synchrotron source, the spectral index, α, is expected to be constant. But from at least September 4 to 6, while the source was transparent at both frequencies, the observations at 2.7 and 8.085 GHz show that the spectral index measurably evolved to its final constant value[5]. Because the source was already transparent at both frequencies well before this evolution occurred, the phenomenon cannot be explained by optical

depth effects. There is also evidence for evolution in α at still higher frequencies. Data at 8.0 and 15.5 GHz (ref. 7) show that the spectrum steepened from $\alpha = -0.44$ to $\alpha = -0.71$ between September 3 and 4. At these frequencies, the source was always transparent so that the question of possible optical depth effects does not even arise. Some additional process must have been at work.

One such process might be absorption of radiation by a plasma. Synchrotron radiation in a rarefied plasma would show a flux density depressed at low frequencies relative to what would be observed for radiation *in vacuo*. Looking at the 8,085 and 2.7 GHz data, I surmise that if the observed 2.7 GHz radiation is to some extent depressed, then α should be closer to zero, less negative than if the particles were radiating *in vacuo* and none of the radiation was suppressed. A larger flux density at the low frequency, than that observed, would change the spectral index in the direction of a larger negative index; that is, toward the constant value one would expect for a transparent source of electrons radiating in a vacuum. The fact that the spectral index evolved up to about September 6 at 8.085 and 2.7 GHz, and was constant after September 6, can be explained by arguing that the plasma was dense enough before September 6 to have noticeable effect and, after September 6, rarefied enough so that its effect dropped from view. If the spectral evolution does find its explanation in this argument, then the turnover in flux density at low frequencies is caused not by synchrotron self-absorption, but by absorption

of the radiation in a dispersive medium[4], the so-called Razin–Tsytovich effect.

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Non-equilibrium Isotopic Fractionation between Seawater and Planktonic Foraminiferal Tests

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Planktonic foraminiferal tests are not formed in isotopic equilibrium with seawater; the deviation is species dependent.

UREY[1] has suggested that the temperature dependence of the isotopic fractionation factor between the oxygen in water and the oxygen in calcium carbonate could be used as a geological thermometer. For estimating Earth surface temperatures, biologically deposited calcium carbonate is more widely available than inorganic precipitates. So it was necessary to discover whether or not organisms deposit carbonate under equilibrium conditions. Epstein *et al.*[2,3] investigated this using molluscs; although they found one case where a mollusc seemed to have deposited some carbonate in non-equilibrium conditions, they ascribed this to special circumstances. Apart from this one case, they inferred that the Mollusca deposit calcium carbonate in isotopic equilibrium with the surrounding water.

Until recently it has been assumed that this is also true of the Foraminifera. Support for this assumption comes from the

seemingly reasonable temperature values which Emiliani[4,5] derived making this assumption. Indeed, whereas the first work on molluscs was performed with the intention of investigating the isotopic fractionation as a function of temperature, the first work on planktonic foraminifera[6] was an investigation of the depth (temperature) habitat of recent foraminifera, performed on the assumption that the isotopic fractionation factor was known. We now find that this was an unwarranted assumption, and that a substantial portion of the variation in isotopic composition between one species and another in foraminiferal death assemblages is due to different fractionation factors rather than to different life habitats.

Oxygen Isotope Analyses

Duplessy *et al.*[7] have previously reported differential isotopic fractionation among benthonic foraminiferal species, and van Donk[8] obtained evidence suggesting that the planktonic species may also deposit calcite out of equilibrium with water. But although a fossil population such as that studied by Duplessy *et al.* enables a comparison to be made between benthonic species, it cannot be used for planktonic species because they do not derive from the same temperature habitat. For this rea-
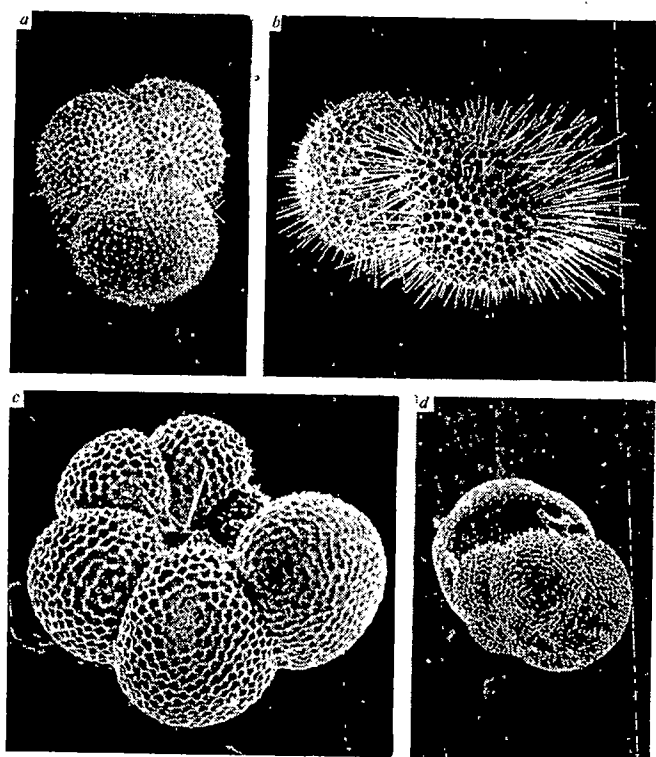
Fig. 1 Electron scanning micrographs of planktonic foraminifera from a 50 m horizontal tow (16° 38′ S, 113° 03′ E). *a, G. ruber* (×65); *b, G. sacculifera* (×65); *c, G. dutertri* (×120); *d, P. obliquiloculata* (×65).

son, it is only possible to compare the departure from isotopic equilibrium among planktonic species if they are collected in plankton tows within the isothermal layer of the ocean.

With the exception of a few samples analysed by van Donk all oxygen isotope analyses of planktonic foraminifera so far published have been performed using fossil or sub-fossil material. The reason is that it is in general difficult to collect large enough samples from plankton tows for conventional isotope analysis. In the present work we have been able to analyse samples as small as 0.04 mg carbonate, and so have been able to make use of a series of plankton tows made in the Indian Ocean by US Coastal and Geodetic Survey Ship Oceanographer in 1967. The stations from which we have used samples in this study are given below in Table 1. Some samples are shown in Fig. 1.

Table 1 Sites of Sampling Stations 150 m Horizontal Tows

BM number	Station number	Latitude	Longitude
1968,0,433	3	08° 11′ N	75° 13′ E
1968,0,434	4	06° 52′ N	77° 43′ E
1968,0,435	5	05° 55′ N	80° 07′ E
1968,0,436	6	05° 34″ N	83° 38′ E
1968,0,437	7	05° 26′ N	85° 37′ E
1968,0,445	15	16° 38′ S	113° 03′ E

Where possible, the samples for isotope analysis were divided and two independent analyses made. This provides a check on the reproducibility of the analyses, which we considered desirable because plankton have not previously been analysed at the Cambridge laboratory. Samples were roasted *in vacuo* for 30 min at 450° C prior to analysis. Carbon dioxide for mass spectrometric analysis was released by the action of 100% orthophosphoric acid at 50° C. The oxygen isotopic composition of the gas was compared with that of an aliquot from a standard bulk gas sample, using the mass spectrometer described by Shackleton[9], and the results calibrated by analysing standard carbonates under the same conditions.

In this work Emiliani's belemnite standard B1 has been used as a calibration standard, assuming its ^{18}O content to be $+0.1\%_{00}$ with respect to the PDB standard. Analyses listed in Table 2 are referred to the PDB standard on this basis. PDB is a standard based on a belemnite from the Carolina Peedee Formation[10].

Table 2 Oxygen Isotopic Composition (δ, $\%_{00}$) of Foraminifera (Fig. 1) from Plankton Tows

Station	G. ruber	G. sacc.	G. dutert.	Pull. obl.
3	−2.69	−2.42	−2.27	−2.08
4	−2.77	−2.50	−2.16	−1.98
5	−2.59	−2.55	−2.15	−2.01
6	−2.64	−2.65	−2.37	−2.36
7	−2.65	−2.69	−2.30	−2.22
15	−2.40	−2.28	−2.14	−1.71

Fourteen of these figures are the mean of two independent analyses. The standard error of a single analysis may be estimated from the difference between these pairs as $\pm 0.11\%_{00}$.

Not all the species in each plankton tow sample have the same isotopic composition. We have performed an analysis of variance to isolate between species, between station and residual variation.

Between species variation proves to be highly significant ($P < 0.001$). The Students T test was used to test variation between species (Table 3).

Table 3 Variation Between Species

G. ruber × G. dutert.	$T = 6.903$ DF 15 significant $P < 0.001$
G. ruber × P. obliqui.	$T = 9.958$ DF 15 significant $P < 0.001$
G. sacc. × G. dutert.	$T = 4.993$ DF 15 significant $P < 0.001$
G. sacc. × P. obliqui.	$T = 8.048$ DF 15 significant $P < 0.001$
P. obliqui. × G. dutert.	$T = 3.055$ DF 15 significant $P < 0.01$

The residual variation is 0.1‰, which may be compared with the standard deviation of $\pm 0.11\%_{00}$ derived from the pairs of analyses. The apparent difference between *G. ruber* and *G. sacculifera* is only 0.11‰, too small to be estimated reliably in the present experiment.

Implication for Depth–Habitat Studies

Emiliani[6], Lidz *et al.*[11] and Hecht and Savin[12] have used $^{18}O/^{16}O$ ratio determinations in foraminiferal tests as a method of investigating their life habitats. In the course of a study of a core in the Indian Ocean, Oba[13] did the same for one sample. It is clear from our study that this is not a valid approach; indeed, as regards the four species discussed here the between species differences found in plankton samples from 50 m horizontal tows are indistinguishable from the variations found by Oba in a sediment sample. This means that in all probability none of the variation measured by Oba can be ascribed to different depth habitat among the four species; they all derive from populations living in the isothermal layer.

In the Atlantic province, larger differences between the species have been measured[6,11,12]; it seems likely that in that case there is a contribution which may be safely ascribed to difference in depth habitat. At the same time we need to know much more about the differential fractionation effect before we can begin to use isotopic determinations in order to deduce life habitat.

Hecht and Savin[12] have gone further, and attempt to use isotopic determinations to discover whether morphological variation within a population of foraminifera is due to varying ecological stress; they deduce, for example, that specimens of *Globigerinoides ruber* with a diminutive final chamber are those

Table 4 Estimated Deviation from Isotopic Equilibrium

| Station | Test | $\delta_w$est. | $\delta_c$est. | Difference between δ_{meas} and δest | | | |
				G. ruber	G. sacc.	G. dutert.	P. obliqui.
3	27°	$+0.1\%_{oo}$	$-2.14\%_{oo}$	-0.55	-0.28	-0.13	$+0.06$
4	27°	$+0.1\%_{oo}$	$-2.14\%_{oo}$	-0.63	-0.36	-0.02	$+0.16$
5	27°	$+0.1\%_{oo}$	$-2.14\%_{oo}$	-0.45	-0.41	-0.01	$+0.13$
6	27°	$0.0\%_{oo}$	$-2.24\%_{oo}$	-0.40	-0.41	-0.13	-0.12
7	27°	$0.0\%_{oo}$	$-2.24\%_{oo}$	-0.41	-0.45	-0.06	$+0.02$
15	25°	$0.0\%_{oo}$	$-1.83\%_{oo}$	-0.57	-0.45	-0.31	$+0.12$
				$-0.50\%_{oo}$	$-0.39\%_{oo}$	$-0.11\%_{oo}$	$+0.06\%_{oo}$

which have lived in deeper (colder) water, by comparing their oxygen isotopic composition with that of normal individuals. Although this seems to be an ingenious test, we cannot exclude the possibility that whatever factor influences the shape of the final chamber also influences the departure from isotopic equilibrium in the test carbonate. This is by no means impossible, particularly because the suggestion made by Parker[14], that non-equilibrium isotopic composition could be causally related to the presence of symbiotic zooxanthellae, has never been excluded.

Implications for Palaeotemperature Studies

Because isotope analysis was not envisaged when the samples were collected, we do not have information on the temperature and isotopic composition of the water in which the foraminifera were living. This means that we cannot estimate exactly the isotopic composition which would have been measured had the test carbonate been deposited in isotopic equilibrium; however, an approximate estimate may be made. Craig and Gordon[15] show that in the equatorial region the observed variation in surface isotopic composition with salinity is small, about 0.11‰ for 1‰ change in salinity. Using Defant's[16] plate V, we may assume that at stations 6, 7 and 15 the salinity was in the region of 34.5‰, and that the isotopic composition of the water was near zero on the PDB scale ($+0.2‰$ on the SMOW scale[15]. At stations 3, 4 and 5 the salinity is likely to have been a little higher and the isotopic composition about $+0.1‰$ on the PDB scale. As regards temperature, the mean August surface temperatures (Defant[16], Plate 3B) are about 27° C for stations 3, 4, 5, 6 and 7, and about 25° C for station 15. Using these estimates and the relation between temperature and isotopic composition given by Craig[17] yields the values in Table 4. Comparison with the measured isotopic composition for each species from Table 2 gives the extent of departure from isotopic equilibrium for each species. The estimates range from $-0.50‰$ for *G. ruber* to $+0.06‰$ for *P. obliquiloculata*.

In column 4 of Table 4 the isotopic composition of carbonates deposited at the temperature given in column 2, and in water having the isotopic composition of column 3, is estimated on the basis of the equilibrium relationship of Craig[17]. The remaining columns are the differences between the measurements from Table 2 and the values in column 4, and thus represent deviations from isotopic equilibrium for the species concerned.

For this last species, the deviation is insignificant; it may well be that this species does in fact deposit its test in isotopic equilibrium with the surrounding water. If one could extract confidently from the sediment only those tests of *P. obliquiloculata* which lived in the isothermal layer of the ocean, this might well be an ideal species to use for palaeotemperature determination; it is possible that these could be recognized by the lack of the smooth external cortex which is a characteristic feature in tests from deeper water.

At the other end of the scale, *G. ruber* yields a value 0.5‰ lighter than it would if isotopic equilibrium prevailed. This is equivalent to an error of about 2.5° C.

Before these values are used to correct estimates of palaeotemperature, it is important to establish whether the "vital effect"[1] remains constant for each species. We have only measured the effect for foraminifera living at 50 m and in a restricted area of an ocean; it is of great interest to discover whether our results have general application.

It is in any case not possible to use the data to correct measurements made in other laboratories because at present results from different laboratories do not seem to be related to each other. For example, specimens of *Globigerinoides sacculifera* from the top of core P6304–8 gave $-1.29‰$ when analysed by Emiliani[6]; samples from the same level in the same core gave $-1.69‰$ when analysed by Lidz *et al.*[11] and the same species from nearby core V12–122 yielded $-2.2‰$ (ref. 18). When corrected for the isotopic composition of the Caribbean water ($+0.92‰$) these figures yield temperatures from near 27° to near 32° C. At present these differences seem more serious than the fundamental problem posed by the present work.

We conclude that whether the isotopic composition of a foraminiferal test is analysed with a view to determining its present-day life habitat, or with a view to elucidating the mysteries of climatic change in the past, it is not possible to translate the value obtained into an equivalent temperature on the basis of thermodynamic principles alone. In some manner yet to be determined the organism deposits carbonate of isotopic composition differing slightly from the thermodynamically predicted value.

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LETTERS TO NATURE

PHYSICAL SCIENCES

Flying Clocks and the Sagnac Effect

IN their "flying clock" experiment[1] Hafele and Keating observed an on-Earth directional dependence of the relativistic time dilation. I have argued[2] that such a dependence is contrary to special relativity theory; the effect, however, is essentially one involving accelerated motion[3] and my neglect of this fact invalidated my argument. None the less, locally the time effects on moving clocks may be regarded as special-relativistic (neglecting the altitude effect, which is not relevant for the present discussion); and the derivation of the effects was made by Hafele with the customary $(1-v^2/c^2)^{\frac{1}{2}}$ time-rate change factor[4,5]. A seeming inconsistency then still arises in considering the clocks from the Earth reference frame: if two similar clocks are moving on equatorial paths with equal speeds relative to the Earth, one westward and one eastward, they should have equal time rates and equal kinetic energies in the Earth system. Evidently, they do have equal energies, but not equal time rates. But if the Sagnac effect is taken into account in the synchronization of clocks in the Earth frame the contradiction disappears; one finds, rather, a further exemplar of consistency in the theory of relativity

With omission of the altitude term, the equation[4] which was confirmed by the Hafele–Keating observation is

$$\Delta t' \simeq (1-v^2/2c^2 - vR\Omega/c^2)\Delta t \qquad (1)$$

Δt is time interval for a rest Earth clock and $\Delta t'$ is for a clock moving on the equator with speed v, $(+)$ for eastward, $(-)$ for westward motion; Ω is the Earth's axial rotation velocity, and R its radius (to be taken with a $\cos \lambda$ factor for east–west motion at latitude λ).

The Sagnac effect[6-8] requires that the time for light to be reflected around a closed path in a system rotating with angular velocity Ω will be longer (shorter) by $2A\Omega/c^2$ than when $\Omega=0$, if the sense of the path is the same as (opposite to) that of Ω; A is the area enclosed by the light path. Synchronizing rest clocks along the equator, using the Einstein procedure[9], requires that $t_2-t_1=L/c$, where t_2 and t_1 are reception and emission times, respectively, for a light signal sent the Earth distance L from clock "1" to clock "2". For signals directed eastward, additional time $2\pi R^2\Omega/c^2$ will be required for traversal around the Earth, compared with the time that would be given by clocks in a hypothetical non-rotating Earth system S. Hence the equatorial clocks fall behind, compared with S clocks, as we progress eastward; the Earth observer, using the $\Delta t=L/c$ criterion, does not take into account the increase in light path that results from the Earth's axial rotation. (The equatorial rest clocks also are presumably running slow by a uniform $\Omega^2 R^2/2c^2$ factor, compared with the S clocks.)

In moving a distance $\Delta x=v\Delta t$ the eastward flying clock should lose $(v^2/2c^2+vR\Omega/c^2)\Delta t$ s compared with Earth rest clocks. But if these are synchronized by the Einstein procedure, an eastward displacement of Δx gives a fraction $\Delta x/2\pi R$ of the $2\Omega A/c^2$ Sagnac loss, which is, using $A=\pi R^2$, a loss of $(\Omega R/c^2)\Delta x$. This decrease is the same as the loss, $(vR\Omega/c^2)\Delta t$, $\Delta t=\Delta x/v$, that is prescribed by equation (1). Hence, the Earth observer will not see a direction time change for the moving clock, but only the kinetic $(v^2/2c^2)\Delta t$ loss. Similarly for a

clock moving to the west: the $(+vR\Omega/c^2)\Delta t$ gain will be compensated by the increase that the Sagnac effect gives to the synchronized clocks. For the Earth observer, then, each flying clock loses time only by the $-v^2/2c^2$ factor.

But at some point there must be a discontinuity of $2A\Omega/c^2$ in the equatorial clock system, because the Sagnac effect puts that loss (gain) into an eastward (westward) synchronization around the equator. The $(vR\Omega/c^2)\Delta t$ term of equation (1), with $\Delta t=2\pi R/v$ for a circumnavigation of the Earth, also gives the time difference $2\pi \Omega R^2/c^2 = 2\Omega A/c^2$, in exact agreement with the synchronization discontinuity. Also, we see from the last calculation that the difference is independent of the speed v at which the clock is moved. Hafele and Keating did confirm a $\pm 2A\Omega/c^2$ time difference (~ 200 ns, $\lambda=0$) for clocks carried around the Earth, compared with a rest clock.

For equatorial clocks set by meridian transit of star (in effect, synchronized with S coordinate clocks), the east–west time effect will appear. With Einstein synchronized clocks there would be no directional effects along a given line of latitude, but there would be what we might call the Hafele–Keating discontinuity, of magnitude $2A\Omega/c^2$ and, like the International Dateline, required for single valued time measure. Because A varies with $\cos^2\lambda$, a continuous change of time would then also be required along each line of longitude. There would be no physical basis in north–south signal propagation for this last time variation. But with any idealized spherical Earth time-mesh there would be a north–south signal insensitive discrepancy; a $(1-\Omega^2 R^2\cos^2\lambda/c^2)^{\frac{1}{2}}$ clock-rate slowing factor that is uniform at any given λ. Seemingly, the asymmetry in clock synchronization that comes with the Earth's axial rotation cannot be escaped.

I thank Professor Peter D. Noerdlinger for a conversation in which he suggested the role of the Sagnac effect elaborated in this letter.

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Possible Marginal Fracture Ridge south of South Africa

A NOTABLE feature of the continental margin south-east of South Africa is its steep slope. Off the west coast of South Africa, north of Cape Town, a thick wedge of sediments has given the slope a gentle gradient of about 1.5° (ref. 1), while southwards from Cape Town the gradient is about 5°. But when the slope turns abruptly (at the tip of Agulhas Bank,

Fig. 1) to face the Indian Ocean, a steep "scarp" of up to 10° is encountered. Seismic profiling data, recently collected by the Geological Survey of South Africa, show that between the Agulhas Bank and Port Elizabeth the steep scarp can be directly related to the presence of a basement ridge beneath the continental slope.

Nine seismic reflexion profiles across the continental margin (Fig. 1) clearly show the nature of the basement ridge. Three of the profiles, numbers 2, 5 and 9, are presented in Fig. 2 as interpretative line diagrams. The ridge is best developed as such in the vicinity of profiles 3, 4 and 5, where it divides the slope into an upper sediment terrace and a lower basement scarp. It reaches a width of about 40 km in this area, and its crest consists of a number of peaks, usually three. It has no magnetic signature. The upper sediment terrace has evolved as a result of the damming effect of the ridge, although on profile 4 sediment seen to be banked up against the southward facing scarp may have spilled over the barrier. Seawards, the basement scarp drops down to a poorly developed continental rise, where a chain of seamounts and small basement peaks runs parallel with the continental slope. Our profiles do not show the relationship of the basement ridge to this seamount chain, but an interpretation of magnetic data (A. P. and E. S. W. Simpson, unpublished) indicates that the boundary between continental and oceanic crust (named the Agulhas Fracture Zone by K. O. Emery, private communication) may run between the two features. The ridge therefore seems to be a basement high associated with the continental crust.
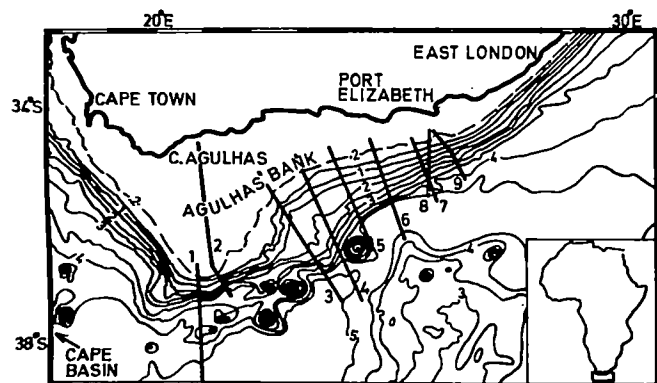
Fig. 1 Bathymetric map of the continental margin south of South Africa. Isobaths are drawn at 200 m and thereafter at 500 m intervals; depths given in km. Locations of the continuous seismic profiles 1 to 9 are marked. Inset shows the position of the area with respect to Africa.

Profiles 6 to 9 show that the crest of the ridge becomes deeper towards the north-east. South of Port Elizabeth it lies at about 3 km below sea level. Between Port Elizabeth and East London, a change in the topography of the lower slope, from being convex in profile to being concave, suggests that the ridge may disappear completely in this region or continue as a very small feature. A linear positive magnetic anomaly, caused by the juxtaposition of continental and oceanic crusts, converges on the ridge east of Port Elizabeth. South-westward from profile 3 the trend of the top of the basement scarp is inferred from bathymetric data until profile 2 is reached. Here the basement rises very steeply to within 1 km of the sea surface before disappearing beneath the sediment cover on Agulhas Bank. At the bottom of the continental slope, basement is lost beneath a trough of sediments presumably associated with the Agulhas Fracture Zone.

We consider the relationship of the newly discovered ridge to the Agulhas Arch[2], a basement antiform trending southeastwards from Cape Agulhas. Fig. 3 shows the outcrop area of the Palaeozoic and Precambrian rocks forming the Arch and isopachs of the approximate depth to basement below sea
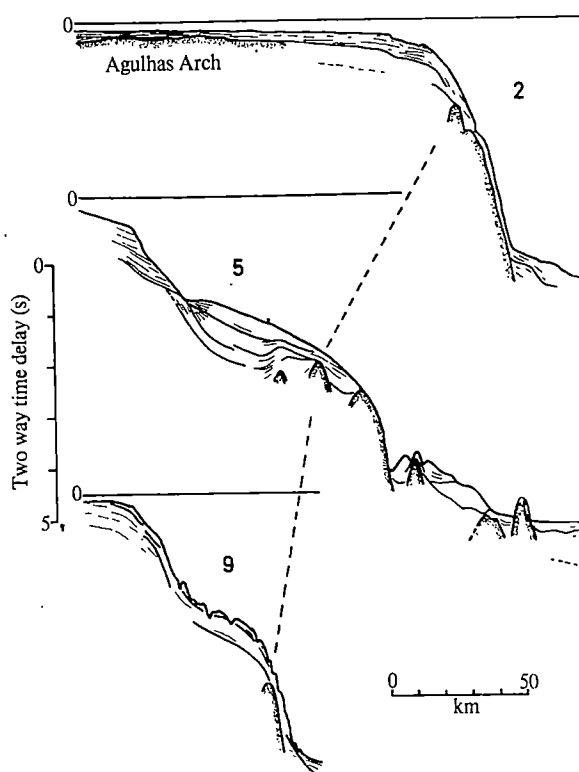
Fig. 2 Interpretative line diagrams of the southern part of profile 2, profile 5 and profile 9. Basement features are stippled. A dashed line correlates the possible marginal fracture ridge from profile to profile.

level in the sediment covered areas (data taken from refs. 2–5 and profile 2). The Arch seems to continue south-eastwards at a fairly shallow depth, less than 1 km, until it meets the basement ridge. Where the two meet, the continental slope is extremely steep, probably as a result of the effect of the Arch on the formation of the ridge. Therefore the two positive features together form a continuous basement high, surrounding the Agulhas Bank and increasing in depth from near sea level at Cape Agulhas to 3 km below sea level near Port Elizabeth. This is an excellent example of a sediment dam[6,7], without which the deep sedimentary basin on the Agulhas Bank[3,8] may not have developed to its present size.
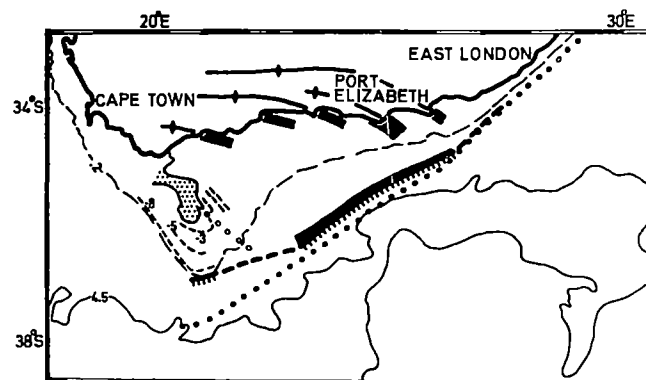
Fig. 3 Structural framework of the continental margin south of South Africa. 200 m and 4.5 km isobaths are shown. Basement ridges have been continued offshore with the aid of seismic data[3]. Magnetic trends taken from unpublished data of A. P. and E. S. W. Simpson. ⟶, Anticlinal axis; ——, basement ridge; ⊓⊓⊓, marginal fraction ridge; ---, inferred ridge; stipple, Agulhas Arch outcrop; . . . , strong magnetic trend; ○○○, weak magnetic trend; depth below sea level (km) to Agulhas Arch marked on contours.

Although there seems to be physical continuity between the ridge and the Agulhas Arch, the age and composition of the former are unknown. Its trend, parallel to the continental edge and oblique to basement trends inshore, suggests an origin associated with the formation of the continental margin. According to a structural model proposed for the South Atlantic[9,10], the margin formed as a line of shear. This took place during the initial opening of the South Atlantic, say between 130 m.y. and 100 m.y. ago, when the Falkland Plateau slid past the Agulhas Bank producing the Agulhas Fracture Zone. On this basis, a Lower Cretaceous age is indicated for the formation of the ridge. The material comprising the ridge could be a splinter of pre-Cretaceous continental basement, perhaps originally attached to the Falkland Plateau. Seismic work has shown that continental rocks underlie the Plateau and its steep northern scarp[11]. Alternatively, the material may be typical of a type of marginal fracture ridge[9], like the Ivory Coast–Ghana Ridge, which is associated with the Romanche Fracture Zone[12]. Structurally, our ridge and the Ivory Coast–Ghana Ridge look similar, and both are magnetically quiet. But the two differ in that our ridge appears to peter out beyond Port Elizabeth instead of running the full length of the continental margin offset (Agulhas Bank to Durban[10]). As a possible explanation for this we suggest that the nature of the continental rocks against which the ridge is formed is a factor governing the size of the ridge. The petering out may then be due to the fact that just north of Port Elizabeth the Cape Fold Belt, underlain by Precambrian basement, dips beneath flat-lying Karroo (Carboniferous to Jurassic) sediments. It may be that the Ivory Coast–Ghana Ridge is better developed because it formed against Precambrian basement throughout its length. An alternative explanation is that our ridge was originally all at one depth but has since sunk differentially.

As yet it is not known if the trend of the newly discovered ridge is continued beneath the sediments of the Cape Basin. Le Pichon and Hayes's theory[9] predicts that a basement high should exist there. Before being sure that we have discovered a true marginal fracture ridge, it is necessary to survey the Cape Basin and satisfactorily explain the petering out beyond Port Elizabeth.

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Palaeolimnology and Palaeomagnetism

MAGNETIC studies of freshwater sediments from northwest England and Northern Ireland have revealed a wide range of applications of magnetic measurements to palaeolimnological studies. They have also shown that lacustrine sediments give a unique record of past changes in the geomagnetic field. This letter is chiefly concerned with the uses of magnetic measurements in helping to interpret lacustrine successions; Creer *et al.*[1] have already discussed the implications of the secular changes of the Earth's magnetic field as recorded in the sediments of Lake Windermere.

The magnetic parameters which have contributed in helping to decipher the information locked in lake deposits are declination, inclination and intensity of the natural (NRM) and cleaned magnetic remanence; initial susceptibility; and response of NRM intensity to a variety of thermoremanent and thermomagnetic tests. Variations in declination with depth can be used to date the sediments. Initial susceptibility and intensity measurements are useful for fine correlations between cores from the same lake, and also provide information about processes which have been operating in the lake's drainage basin. Other magnetic studies have provided information principally about the origin of the material holding the NRM. Instruments have recently been developed at Newcastle to measure the important properties of magnetic declination and its intensity[2,3] and initial susceptibility (L. Molyneux and R. T., unpublished) on whole lengths of core. All samples were collected by Mackereth pneumatically operated piston corers of either 1, 3 or 6 m length[4,5].

The record of secular variation for Lake Windermere is accurately known for the past 11,000 yr (Fig. 1) with a time scale provided by a suite of radiocarbon dates. Fourier and spectral analyses of the results revealed a single significant periodicity of about 2,800 yr in the declination variations, but
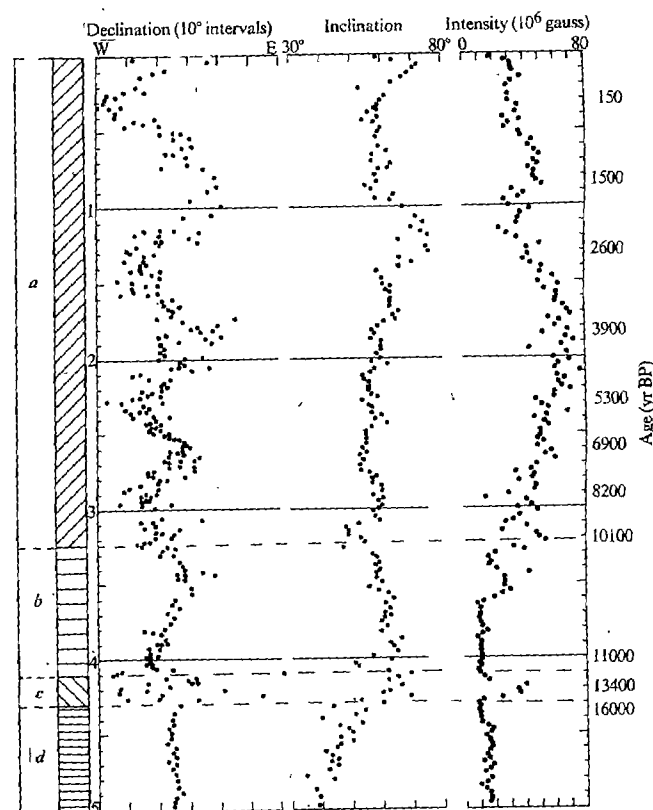
Fig. 1 Composite plot of stratigraphy: declination, inclination and intensity of the NRM versus depth in metres from four 6-m cores of sediment from Lake Windermere. Ages from Mackereth[6]. Relative, rather than absolute, values of declination are plotted. *a*, Post-Glacial organic; *b*, late glacial laminated clays; *c*, amelioration period; *d*, glacial varved clay.

none in the inclination changes (Fig. 2), confirming Mackereth's conclusion[6] that the oscillations in declination were of constant frequency. Comparison of detailed measurements from the top metre of sediment in Windermere with observatory and archaeomagnetic results for the past 500 yr showed that the NRM became stabilized soon after the time of deposition of the sediment, and alternating field cleaning showed that the NRM was of high stability[1]. Thus the Windermere record of declination changes (Fig. 1) provides a reference curve which can be used to date other lacustrine successions simply on their variations in declination of magnetic remanence.
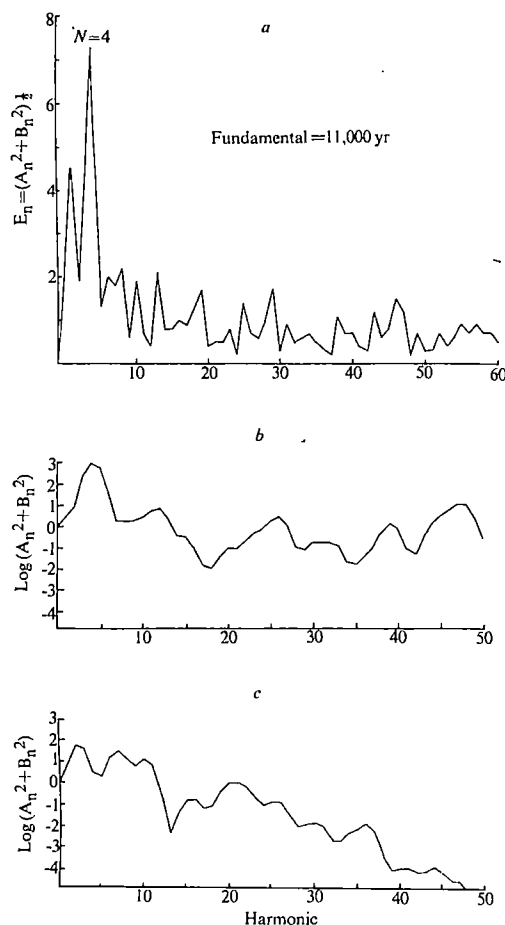
Fig. 2 Lake Windermere. a, Fourier analysis of the declination record; b, spectral analysis of the declination record; c, spectral analysis of the inclination record.

One 6-m and eight 3-m cores from Lough Neagh were provided by F. Oldfield for magnetic measurements from a larger collection intended for palaeobotanical studies. Carbon 14 ages[7] have been assigned to core AB9 by correlating its pollen assemblages with those of another Lough Neagh core which had been isotopically dated. Only the carbon 14 ages of 4,800 and 3,400 BP are now thought to be reliable estimates of the sediment age. These ages compare well with the palaeomagnetic dates (Fig. 3a). Further, pollen analyses yield an age of about 6,000 BP for the basal material in core AB9, in good agreement with the magnetic age. Other cores gave similar swings in declination (Fig. 3b, c) indicating comparable rates of deposition to those in core AB9, but one core (AB11) held more swings in declination than the other cores (Fig. 3d). Comparison with the Windermere reference curve suggests an age of about 9,000 yr BP for the oldest sediment in this core, and shows that the rate of deposition has been markedly slower in the lower half of the core compared with the upper part. Pollen analyses conform remarkably well to this pattern and time scale of deposition[8].

Mackereth (personal communication) showed that the horizontal intensity of the NRM in Windermere was related
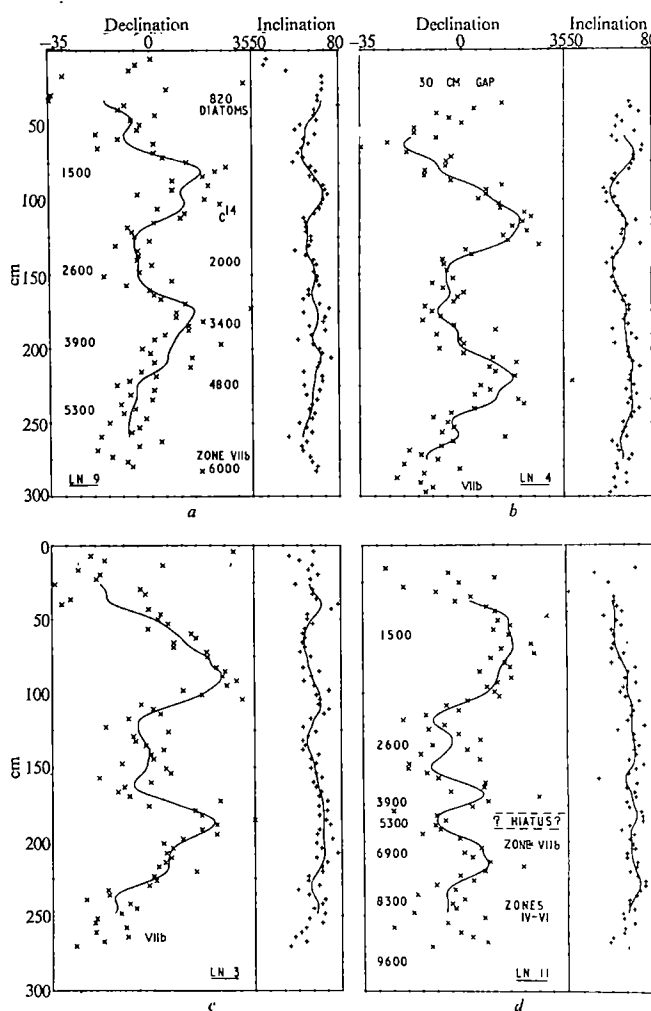
Fig. 3 Declination and inclination changes for four 3-m cores from Lough Neagh. In diagram a the left hand dates are derived by comparison with the Lake Windermere magnetic record, the right hand dates are from Lough Neagh. In diagram d the dates are derived from the Lake Windermere magnetic record.

to the carbon content of the sediments. Measurement of the total intensity of NRM of both Lough Neagh and Lake Windermere sediments again produced the same relationship of direct proportionality between carbon content and intensity. This is a clear indication that the intensity of the remanence was controlled by biological activity in the lake and in particular in the soils of the surrounding areas, rather than by changes in intensity of the geomagnetic field. There is an inverse correlation between the mineral content of the lake sediments and the intensity of their magnetization. For example, in both Lake Windermere (Fig. 1) and Lough Neagh the intensity of NRM reached a maximum in mid-Post-Glacial times, when erosion was at a minimum, but leaching of soils and lake productivity were at a maximum[9]. Thus the remanence is of a chemical, as opposed to a depositional, origin. Low temperature transition studies have shown that the NRM is largely carried by haematite[1].

Initial (low field) susceptibility measurements were made on all the subsamples from the Lough Neagh cores. Sediments from deeper water areas had lower values and smaller fluctuations of susceptibility than the cores from the shallower water nearer the edge of the Lough. The changes in susceptibility of the deep water cores (Fig. 4) were similar from core to core and give a method of accurate correlation between cores in the Post-Glacial organic material, which without detailed analysis seems homogeneous. Correlation with the shallow

water cores is also possible but it is not as precise. Oldfield (personal communication) has demonstrated that the course of susceptibility change (Fig. 4) closely parallels the sequence of forest clearance in the Lough Neagh drainage basin, as reflected in the grass, bracken and rib-wort plantain pollen content of the cores. This aspect of the palaeolimnological work is being pursued in greater detail by magnetic, chemical and botanical investigations of the most recent sediments in Lough Neagh.
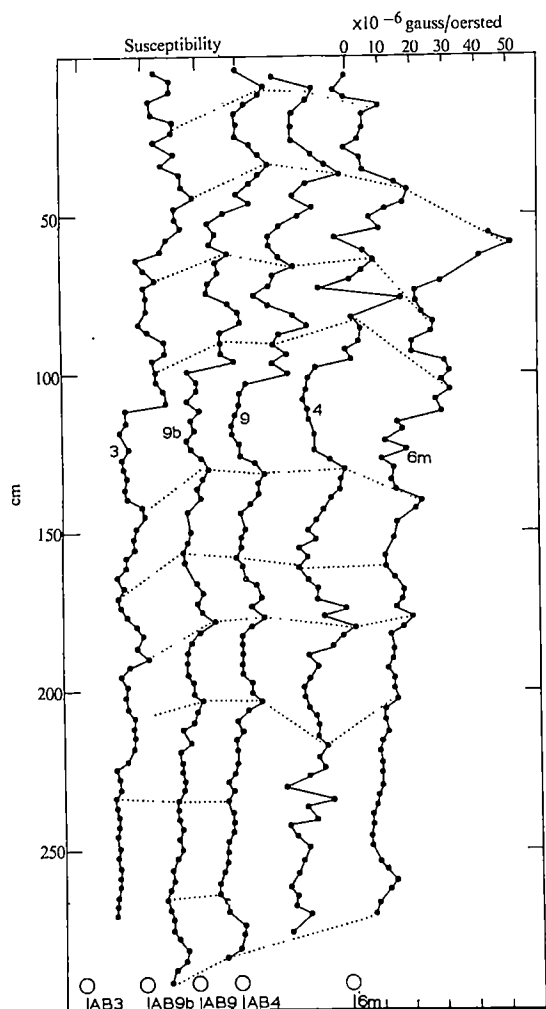
Fig. 4 Susceptibility against depth for the deep water Lough Neagh cores. Susceptibility is plotted on a linear scale: the origin of the susceptibility scale for each core is indicated along the bottom axis. Correlations between cores are shown by the dotted lines. (For comparison with Fig. 3 add 40 cm to depths in core AB4.)

The detailed information about the past changes of the geomagnetic field obtained from Lake Windermere sediments can thus be used to help in the investigation of other Post-Glacial lacustrine deposits. Measurements of changes in declination, particularly using the whole core method, form an extremely rapid dating technique. Declination and intensity variations are useful as reconnaissance tools for providing, nondestructively, stratigraphical information about cores before more detailed and time consuming investigations are carried out. Susceptibility and declination changes give a means of correlating accurately between cores from the same lake. Information about the sediment type, and the biochemical conditions in which it was formed and deposited, are provided by the magnitude of initial susceptibility and intensity of NRM. Present studies on lacustrine sediments from a previous (Hoxnian) interglacial period indicate that the work can be extended further back into the Pleistocene.

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Radiometric Traverse of the Seabed off the Yorkshire Coast

SURFACE and airborne radiometric surveys carried out over land areas during the past twenty years have shown that in addition to locating radioactive mineral deposits they are able to differentiate between the common types of rocks and sediments. As yet, however, few attempts have been made to extend radiometric techniques to the sea floor and, as far as we know, none of these has included *in situ* seabed gamma spectrometry. Bastin[1] towed a gamma ray detector across recent sediments off the Belgian coast and was able to delineate areas of muds, sands and clays. Summerhayes et al.[2], in the course of a study of phosphorite deposits off NW Africa, also made total gamma measurements at a number of sampling stations upon the continental shelf and slope. Subsequent analysis of the samples showed that anomalous radioactivity could be related to the phosphate content of the sediments. Almost all other seabed radioactivity measurements have been connected with the use of radioactive tracers to determine sediment movement.

We have used a towed seabed gamma spectrometer[3] to produce continuous profiles of the natural radioactivity of rocks and sediments on the sea floor. Total count, potassium, "uranium" and "thorium" measurements were made to investigate the possibility of using this technique to map the solid and drift geology. The seabed instrumentation comprises a 76×76 mm NaI(Tl) scintillation detector and EHT unit shock mounted in a 127 mm diameter stainless steel probe. This is attached to 850 m of double-armoured coaxial cable, the lowest 25 m of which is enclosed in a flexible hose of the same diameter as the probe to minimize the risk of snagging on seabed obstacles. The complete unit or "eel" is designed to be towed in contact with the sea floor at speeds of 3–4 kt in depths of up to 200 m.

The shipboard installation is based on Harwell 2000 series electronics with four channels whose energy limits in the present measurements were >0.05 MeV (total), 1.3–1.6 MeV (K), 1.65–1.95 MeV (U) and 2.3–3.3 MeV (Th). Channel outputs were recorded in both analogue and digital form, the energy calibration being maintained by monitoring the 1.46 MeV ^{40}K peak with a 100 channel analyser.

Preliminary sea trials of the spectrometer were carried out on MV Surveyor (NERC charter) around northern Britain between August and October 1971 and included a traverse along the 30 fathom line off the Yorkshire coast (Fig. 1). This commenced 11 km east of Flamborough Head

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and continued in a NW direction parallel to the shore for a distance of about 80 km to the vicinity of Whitby. The traverse was undertaken to test the "eel" upon a moderately uneven rock bottom and to determine whether the radiometric profile would reflect the known lithology of the sea floor.

The solid and drift geology of the area has been described by Dingle[4,5], who has shown that near the coast Triassic to Cretaceous sedimentary formations are well exposed and gently folded into a series of domes and basins. The present traverse crossed two of these structures, the Scarborough Dome and Mallard Basin (see Fig. 1), with the result that the Jurassic succession between the Lower Lias and the Corallian is repeated three times along its length.

The total count, "uranium" and "thorium" profiles recorded along the traverse together with the solid geology are given in Fig. 2. The first is a simplified representation of the ratemeter chart recording and the radioelement profiles have been compiled from successive 500 s scaler counts which were accumulated between the consecutively numbered Decca Navigator position fixes taken at 10 min intervals. The Compton scattering contribution to the "uranium" channel from higher energy "thorium" radiation is not known accurately for the seabed geometry, but we have made an approximate correction to the data on the basis of laboratory measurements with a point source.

The three-fold repetition of the stratal succession is clearly mirrored by the radiometry (Fig. 2). The count rate rises from a minimum over the two Middle Jurassic-Corallian outcrops (fix Nos. 187–191, 216–222) to peaks (198, 208–210, 228) near the Middle-Lower Lias boundaries and fluctuates at an intermediate level (199–206) upon the Lower Lias. These variations are consistent with the lithologies traversed. The Middle Jurassic-Corallian beds are composed predominantly of weakly radioactive freshwater sandstones and shales and marine limestones. The very deep troughs at fix Nos. 188 and 216 may be due to these limestones. In contrast, the Lias is formed mainly of relatively strongly radioactive marine shales with limestone bands which
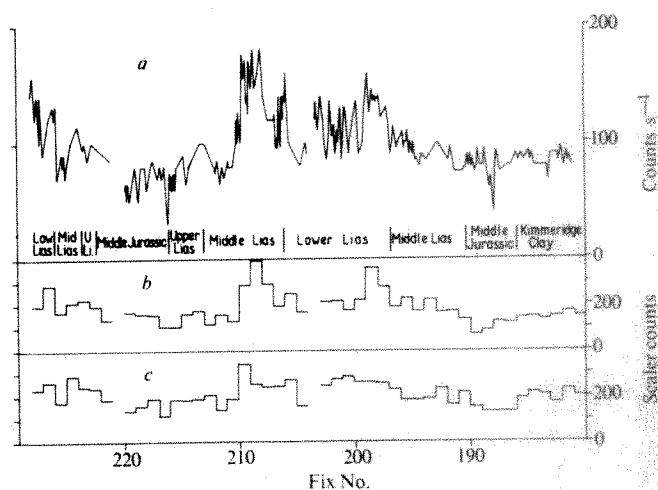
Fig. 2 Total count (a), "uranium" (b) and "thorium" (c) profiles along Yorkshire coast traverse. Each radioelement scaler count was accumulated for 500 s. Middle Jurassic subdivision represents Middle Jurassic-Corallian of Dingle.

increase in number towards the base of the formation. This shale-limestone alternation may account for the large closely spaced fluctuations in the Lower Lias total count record. The radioelement profiles indicate a marked increase of the U:Th ratio at each of the major total count peaks on the Lias and also show a general predominance of thorium over uranium on the Middle Jurassic-Corallian. These relative abundances are characteristic of marine shales and arenaceous deposits respectively.

Although the Jurassic rocks are generally well exposed, Dingle has mapped three drift covered areas along the traverse. The largest of these is a layer of glacial till which completely blankets the Kimmeridge Clay outcrop (181–7) and is presumably responsible for the relatively flat profiles in all three channels. Similar count rates were obtained between fix Nos. 210 and 211 where till overlies Lias shales, and this probably accounts for the abrupt decline in all three channels at this point. The third drift area (216–7) is of sand, which undoubtedly contributes to the very low count rate near fix No. 216.

Although the overall fit between the geology and radiometry is reasonable there are some discrepancies, most notably between the mid-traverse total count peaks and the divisions of the Lias. This could be due partly to the limitations of position fixing as well as to a lack of detailed knowledge of the seabed geological succession.

The geometry of the detector relative to the sea floor is not constant and the channel counts depend in a direct way on the smoothness of the seabed and the depth of the furrow cut by the "eel" as well as on the natural radioactivity of the sediments. Without repeating the measurements along the same traverse it is not possible to be sure that the probe was in contact with the seabed at all times. For example, near fix 216 the count rate is very low and is probably due to an area of sand overlying limestone, but there may have been some loss of contact with the sea floor here also. The gaps in the records at fixes 204 and 221 occur where the "eel" was raised from the seabed to avoid known obstacles.

The detailed evaluation of the pattern of gamma activity and a better understanding of the significance of many of the finer details of these results must await a further and more systematic survey of the area. Similarly a proper analysis of the radioelement channel data requires a careful calibration of the spectrometer on beds of known U, Th and K content. But our results suggest that radiometric techniques offer a valuable new means of extending our knowledge of both the solid and drift geology of the sea floor.
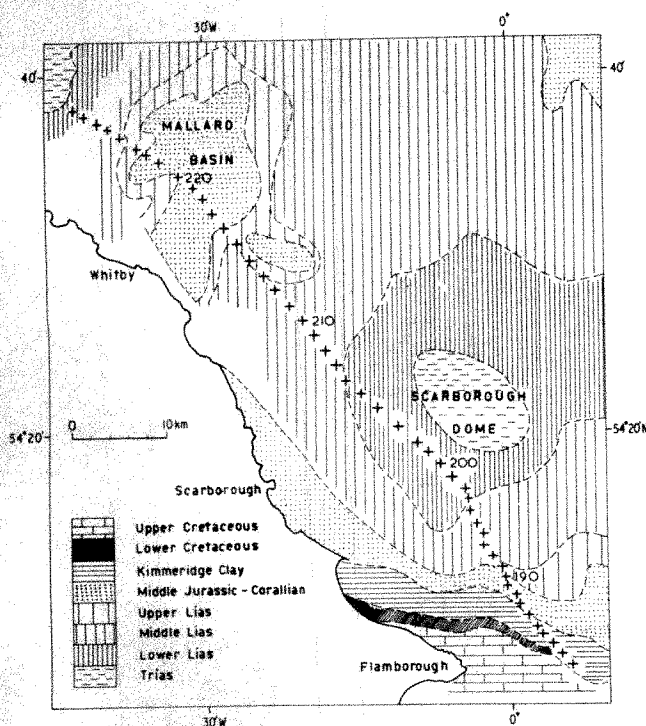
Fig. 1 Plan of Yorkshire coast radiometric traverse. The Decca Navigator position fixes taken at ten minute intervals are marked by crosses. Geology after Dingle[4].

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Radiometric Dating of the Ubeidiya Formation, Jordan Valley, Israel

THE Ubeidiya Formation[1] is known from three localities (Fig. 1) within the Jordan Valley, where it is steeply tilted, faulted and folded[2,3]. It is rich in prehistoric remains, representing the Developed Oldowan and Early Acheulean[4]. The Ubeidiya Formation is important in the Pleistocene history of the Jordan Valley for two reasons: it is the youngest sedimentary sequence to be severely affected by tectonic movements of the graben, and it contains the oldest human implements ever found in the Middle East.
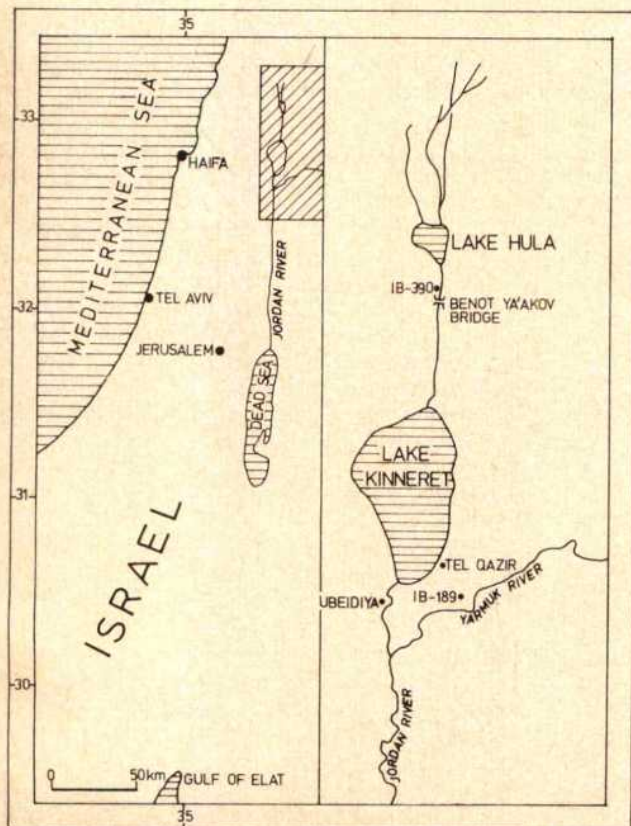
Many inferences concerning the age of the Ubeidiya Formation have been published since it was first described by Blanckenhorn[5]. Blanckenhorn, and later Picard[6], tended to accept a Pliocene age. Picard[2], Picard and Baida[1,7] and Stekelis et al.[8] regarded the formation as of "Lower Pleistocene or Villafranchian" age, a contention based chiefly on concepts regarding its tectonic position. Horowitz[8] discussed the possibility of a Middle Pleistocene, approximately Mindel, age of the Ubeidiya Formation, which was also accepted by others[9-11]. The assumption of a Mindel age was based principally on palynostratigraphic correlation with deep boreholes drilled in the Dead Sea area[12]. ^{230}Th/U analyses were applied by Bender and Kaufman[13] in an attempt to determine the age of the Ubeidiya sediments, but no significant results were forthcoming.

The type-section for the Ubeidiya Formation[7] is described from the vicinity of the site of Ubeidiya (Fig. 1), about 3 km south-west of Lake Kinneret, in the central Jordan Valley. The sequence comprises lacustrine, fluviatile and terrestrial sediments, in which two chief cycles have been distinguished, alternating from lacustrine to fluviatile conditions.

Fig. 2 Outcrop of Mishmar Hayarden Basalt, from which specimen IB-390 was collected.

Two other outcrops (Fig. 1) were ascribed by Picard[2] to the Ubeidiya Formation: one comprises a series of tilted freshwater sediments, cropping out near Tel Qazir, to the east of Lake Kinneret, and the other is located near Benot Ya'akov Bridge (*Jisr Banat Yaqub* in Arabic, as was previously described) on the bank of the Jordan River north of Lake Kinneret. The latter outcrop was described in detail by Horowitz[14], who also found a basalt sheet intercalated within the sediments, which were given the local name Mishmar Hayarden Formation. The three outcrops were ascribed by Picard[2] to the Ubeidiya Formation chiefly because of their structural position—"tilted freshwater series". This assumption was later strengthened by pollen analyses[14], which indicated a great similarity of the pollen spectra in the Benot Ya'akov and Ubeidiya outcrops, and also by the fact that some artefacts turn up in the Benot Ya'akov outcrop. As the number of artefacts is too low, however, it is not possible to make detailed comparisons between them and the rich assemblages of Ubeidiya.

In Ubeidiya itself there are more than ten artefact-containing layers[10] producing different assemblages. These are defined as Developed Oldowan and Early Acheulean, following the terminology of M. D. Leakey[15,16]. In European terminology these would, apart from one assemblage, correspond to the Abbevillian (=Early Acheulean in African terminology). We have carried out K-Ar measurements on a sample of the Mishmar Hayarden Basalt, collected from the outcrop near Benot Ya'akov Bridge (Fig. 2). The rock, specimen IB-390, is a fresh, massive, non-vesicular olivine basalt.

Fig. 1 Location map.

From the analytical data presented in Table 1, we have calculated an age of 640,000 ± 120,000 yr, the error representing analytical uncertainty. Details of analytical methods and constants employed, as well as the regional setting of the Cainozoic basalts of northern Israel, are given in Siedner and Brenner[17].

Table 1 Analytical Data, Calculated Ages and Locations for Dated Basalts from Northern Israel

Specimen and location	K (wt %)	Rad ^{40}Ar ml. 10^{-6} STP per g	Rad ^{40}Ar / Total ^{40}Ar (%)	Calculated age ± error (yr)
IB-390. Basalt, near Benot Ya'akov Bridge (elevation + 100 m a.s.l.)	0.938	0.0239	0.88	640,000 ± 120,000
IB-189. Basalt, above Yarmuk River (elevation + 220 m a.s.l.)	0.709	0.0190	4.9	680,000 ± 50,000

The correlation of the Mishmar Hayarden Basalt with the Yarmuk Basalt, suggested by Horowitz[14] on stratigraphic grounds, is corroborated by their radiometric ages (Table 1). A sample of the latter (specimen IB-189) has yielded an age of 680,000 ± 50,000 yr, which coincides, within the limits of experimental error, with that of the former.

A deep borehole, Melech Sedom 1—drilled in the centre of the Dead Sea basin which serves as the ultimate erosion base-level for the Jordan Valley—penetrated about 4 km of Pleistocene sediments. These were analysed palynologically[12], and indicated four or five alternations of pluvial and interpluvial conditions. The upper two are correlated with outcrops of Würmian and Rissian age, whereas the third and possibly the fourth are correlated with the Ubeidiya Formation. The assumption that the Ubeidiya Formation, taking into account its two limnic and fluviatile cycles, might have been deposited during Günz and Mindel times, has been discussed by Horowitz[8]. We are not sure, however, whether the lower part was deposited through Günz times. It seems that, at any rate, the upper part of the Ubeidiya Formation was deposited during Mindel times.

The Early Acheulean in East Africa is dated as early as 1.5 m.y., extending to about 0.1 m.y. (ref. 18). There is a time gap of about a million years between the East African Acheulean occurrences and the earliest Abbevillian industries in Western Europe, dated as Mindelian in age. There are several hints that the absolute chronology used in the European literature, in the absence of radiometric datings, is perhaps too low[18]. The evidence from Ubeidiya Formation, which dates the Early Acheulean in the Jordan Valley, as probably earlier than Mindel, seems to reveal the antiquity of this culture in Asia.

The dated basalt flow from Benot Ya'akov Bridge is clearly part of the upper section of the Ubeidiya Formation. Its age of 640,000 yr should, therefore, be considered as an approximate minimum age for Mindel times.

As mentioned, the Ubeidiya and Mishmar Hayarden formations were strongly affected by tectonic movements. Rissian sediments, the Benot Ya'akov Formation[14], unconformably overlie the tilted Mishmar Hayarden Formation in the Benot Ya'akov Bridge area. It seems therefore that the tectonic movement which caused the tilting of the Ubeidiya Formation occurred some time within the Mindel-Riss Interpluvial and is younger than 640,000 yr. The use of the terms "pluvial" and "interpluvial" and the application of the alpine names to the local time-stratigraphy are discussed by Horowitz[19] and are adopted here.

Palaeomagnetic analysis of the Mishmar Hayarden basalt, carried out in the field on a number of samples using brunton compass, shows that it cooled under conditions of normal polarity. This coincides well with the radiometric age, corres-

ponding most probably with the Brunhes Normal Epoch that commenced some 700,000 yr ago.

A radiometric dating programme to extend the present preliminary investigation to other Quaternary areas and formations in northern Israel will be commenced shortly.

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The Structure of Powdered Quartz

DIFFERENTIAL thermal analysis (d.t.a.) of quartz normally reveals an endothermic peak at 573° C, corresponding to the inversion from low quartz to high quartz. If the quartz is subjected to grinding it is observed that the peak size decreases, both in height and area; this effect is usually attributed to conversion during grinding of quartz to some amorphous or vitreous form of silica, as has been described by Dempster and Ritchie[1].

Using a quartz sand from Chatteris, Cambridgeshire, we have studied the effects of grinding for various periods up to 400 h on the d.t.a. peak at 573° C. Samples were prepared in a vibration mill with a steel chamber; d.t.a. traces were recorded at a heating rate of 10° C min^{-1}. Fig. 1 shows that after 400 h milling the peak has vanished, and by the accepted theory this sample should consist entirely of some amorphous phase of silica. This sample was found, however, to have the X-ray structure characteristic of crystalline quartz. X-ray powder pictures are given in Fig. 2a and b for quartz milled
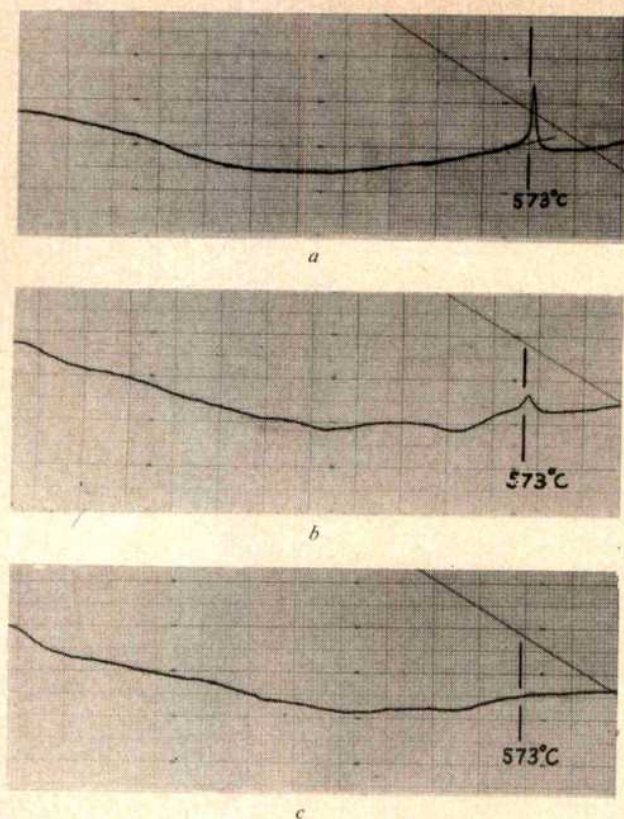
Fig. 1 D.t.a. curves for quartz showing decrease in size of inversion peak at 573° C with milling. a, Original quartz sand; b, milled 100 h; c, milled 400 h.
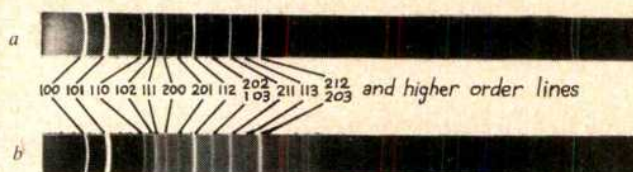
Fig. 2 Debye Scherrer X-ray powder patterns for: a, quartz milled 10 h; b, quartz milled 400 h, showing that the latter has the structure of crystalline quartz as opposed to an amorphous material. (CuK$_\alpha$ radiation, Ni filter.)

10 h and 400 h respectively, and the former may be regarded for purposes of comparison as a reference picture of quartz. The intensities of the low angle diffraction lines revealed that the quartz milled for 400 h consisted of at least 75% crystalline quartz, the diffuse nature of the higher angle lines being a well known effect of either crystal strain or small particle size. In addition, these samples of powdered quartz were found to contain up to 4% by weight of H$_2$O, absorbed from the atmosphere during milling (Fig. 3).

That water is absorbed by quartz during grinding was reported as early as 1908 by Hillebrand[2]. He ground quartz for 3 h in an agate-mortar and found that the loosely held moisture (liberated below 105° C) increased from zero to 0.35% and the firmly held water (liberated above 105° C) increased from 0.06 to 0.45% by weight. This important work of Hillebrand appears to have been overlooked by recent investigators in this field of research.

Impurities introduced from the steel chamber and balls during milling may affect the experiment in several ways. First, iron oxides increase the affinity of silica for water and might have caused the absorption of the large quantities of H$_2$O during milling. Second, Keith and Tuttle[3] attributed variations in the temperatures of inversion and sluggishness of inversion of specimens of quartz from different sources to the solid solution of impurities in trace amounts: thus the

impurities introduced by milling might have accounted for the decrease in size of the d.t.a. inversion peak.

Another technique of grinding resulting in a different impurity contamination was therefore employed. Electronic grade Brazilian quartz was milled for a period of 500 h in a small agate-mill. The resulting sample evolved 5% by weight of H$_2$O on heating to 800° C, and did not exhibit the d.t.a. inversion peak characteristic of quartz. Thus the absorption of water vapour and disappearance of d.t.a. inversion peak appeared independent of impurity. To check if the ability to invert at 573° C to high quartz had been suppressed, this material was examined in a Lenne camera, which gives a continuous record of X-ray structure versus temperature. Lenne diagrams for Brazilian quartz agate-milled 5 h (reference material) and Brazilian quartz agate-milled 500 h are shown in Fig. 4a and b respectively.

Both diagrams are very similar. There is a gradual change of slope of the diffraction lines owing to thermal expansion of the samples: lines labelled "Pt" are due to the platinum specimen holder. At 573° C there is a sudden discontinuity of the lines owing to the 0.86% volume expansion which accompanies inversion from low quartz to high quartz, which appears less sharp for the quartz milled 500 h. Also the III line was absent for both samples above 573° C, which is further evidence that both samples change from low to high quartz. Thus although the quantity of quartz detectable by d.t.a. becomes less during grinding, it is apparent that the resultant product still has the structure of low quartz which changes to high quartz when heated through 573° C.

Thermal conductivities of the samples were measured by Lee's disk method for samples packed to the same degree as for the d.t.a. (Fig. 5), and were found approximately independent of milling after the first few hours. The decrease in size of the d.t.a. peak is therefore not due to changes of thermal conductivity.

We determined the densities of samples withdrawn from the steel vibration mill using specific gravity bottles and water as the working fluid (Table 1). Two corrections were made: first, for absorbed H$_2$O (making the assumption that the absorbed H$_2$O effectively has the same density as liquid water at the same temperatures); second, for the presence of iron contaminant (measured by flame spectroscopy and by hydrogen displacement from acid). The average of the corrected values comes to 2.650 ± 0.012 g ml.$^{-1}$, close to the value for quartz which is 2.650 g ml.$^{-1}$ at 25° C. Therefore it appears that the observed changes in the measured density were adequately
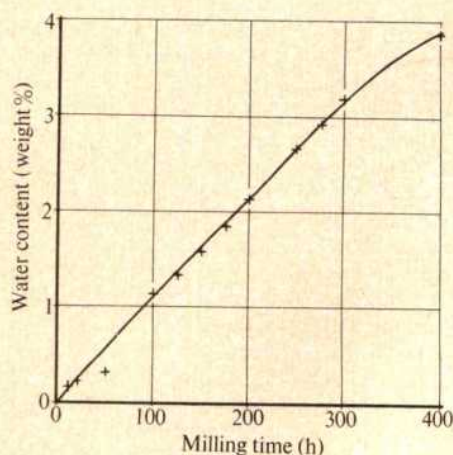
Fig. 3 Relation between water content of powdered quartz and duration of milling. The water contents were determined from the loss of weight on heating to 800° C, checking that the loss in weight was equal to the quantity of water condensable from the evolved vapours. Although samples could be heated to constant weight at lower temperatures they retained a certain fraction of absorbed H$_2$O which could only be driven off by heating to 800° C.

Table 1 Density Results for Powdered Quartz at 25° C

Milling time (h)	Measured density (g ml.$^{-1}$)	Density corrected for the presence of moisture only (g ml.$^{-1}$)	Density corrected for the presence of water and iron impurity (g ml.$^{-1}$)
0	2.643	2.643	2.643
10	2.656	2.663	2.656
20	2.654	2.663	2.650
50	2.649	2.662	2.643
100	2.630	2.680	2.655
125	2.621	2.680	2.655
150	2.606	2.675	2.647
175	2.592	2.673	2.643
200	2.577	2.669	2.638
250	2.574	2.691	2.658
275	2.559	2.686	2.651
300	2.543	2.680	2.644
400	2.540	2.710	2.678

Density of quartz at 25° C = 2.650 g ml.$^{-1}$ Mean = 2.650 g ml.$^{-1}$
s.d. = ± 0.012 g ml.$^{-1}$

Fig. 5 Thermal conductivity data for powdered quartz.

explained in terms of the absorbed H_2O and iron introduced during milling.

It is important to note the drying procedure used by those investigators who have reported falls in density of quartz during powdering. Ray[4] employed a temperature of 150° C and found the density of a silver sand to fall from 2.638 to 2.528 g ml.$^{-1}$ during milling; he concluded that as much as 25.7% of the quartz had been converted into vitreous silica. This agreed well with a value which he obtained from the heats of solution. Sosman and Merwin[5], however, repeated Ray's work, but optical examination revealed that the powdered quartz was still completely crystalline.

Dale[6] pointed out that Ray had not taken into account contamination by agate during milling. He found that although the density of quartz decreased during grinding, part of the fall could be accounted for by such contamination

Fig. 4 Lenne diagrams of milled quartz. *a*, Quartz milled 5 h; *b*, quartz milled 500 h. Lenne pictures give plot of X-ray structure against temperature. The inversion of the quartz milled 500 h appears less sharp than the inversion of the quartz milled for 5 h.

(density of agate ~ 2.60 g ml.$^{-1}$). If, however, the remaining reduction of density was due to the conversion of the quartz to vitreous silica (2.2 g ml.$^{-1}$), then this amounted to only a few per cent as compared with Ray's 25.7%. Dale employed a temperature of 200° C for drying his samples.

Our finding that heating at 800° C is necessary to drive off all the water from the samples of quartz suggests that the drying temperatures of 150° C and 200° C reported above were inadequate and the samples would have contained some H_2O still in combination.

Clelland and Ritchie[7] found an increased initial solubility and decreased density for quartz when powdered. They rejected hydration as an obvious possibility, because of differences in the solubility characteristics between powdered quartz and silica gels. They concluded that the surfaces of the quartz particles had become converted to "vitreous silica of the Beilby type produced by melting and surface flow". Dempster and Ritchie[8] also found a reduction in density after grinding, but not as large as that reported by Clelland and Ritchie. They attributed this partly to the effects of impurities and partly to the "more rigorous drying of the dusts before weighing (110° C, 4 h)"; again, our results suggest that their drying procedure was inadequate.

Sakabe[9], using a drying temperature of 150° C, found that the longer the quartz was ground, the more intense were the OH infrared absorption bands. Also, Soda[10] concluded that the silanol group exists in the surface structure of powdered quartz.

Thus there is considerable evidence that quartz absorbs atmospheric moisture during powdering, but it does not appear to have been pointed out that this is the most probable reason for the decrease in density of quartz produced by milling.

Further research suggests that the disappearance of the d.t.a. inversion peak at 573° C with milling is due to a spreading of the inversion over a small range of temperature. When d.t.a. is carried out at about twice the normal heating rate, at 18° C/min, the "lost" d.t.a. peak again becomes quite pronounced, possibly because the effect of a dispersion of the inversion over a small range of temperature becomes less and a greater fluctuation of differential temperature is produced. When d.t.a. is carried out at low rates of heating, each fragment of quartz inverts at its own individual inversion temperature, and more time is available for heat to be conducted to the sample as a whole, giving rise to a smaller inversion peak.

It would appear that when quartz is powdered, it acquires properties which would classify it as a "microform". According to Sosman[11], fine subdivision and twinning may so alter the properties of a phase of silica that it can no longer be readily identified, even when it forms the basis of an aggregate. Sosman has called them the "microforms" of silica, and their obscurity is almost entirely due to their fine grain size. Sosman has classified the microforms of silica into microcrystalline,

microamorphous, and microaphanitic, and further on a geometric basis into microgranular, microlamellar, and microfibrous. More recently, Kloss[12] reported that, unlike macrocrystalline quartz crystals, microcrystalline quartz crystals generally show no sharp inversion point, and the inversion takes place over an interval of nearly 50° C. Our work suggests that it is best to describe the product of powdering quartz as microcrystalline quartz, which has an X-ray structure corresponding to quartz but is not normally detectable by d.t.a. unless carried out at high heating rates. In addition, this microcrystalline quartz contains chemisorbed H_2O.

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Image Formation by Induced Local Interactions: Examples Employing Nuclear Magnetic Resonance

An image of an object may be defined as a graphical representation of the spatial distribution of one or more of its properties. Image formation usually requires that the object interact with a matter or radiation field characterized by a wavelength comparable to or smaller than the smallest features to be distinguished, so that the region of interaction may be restricted and a resolved image generated.

This limitation on the wavelength of the field may be removed, and a new class of image generated, by taking advantage of induced local interactions. In the presence of a second field that restricts the interaction of the object with the first field to a limited region, the resolution becomes independent of wavelength, and is instead a function of the ratio of the normal width of the interaction to the shift produced by a gradient in the second field. Because the interaction may be regarded as a coupling of the two fields by the object, I propose that image formation by this technique be known as zeugmatography, from the Greek ζεύγμα, "that which is used for joining".

The nature of the technique may be clarified by describing two simple examples. Nuclear magnetic resonance (NMR) zeugmatography was performed with 60 MHz (5 m) radiation and a static magnetic field gradient corresponding, for proton resonance, to about 700 Hz cm^{-1}. The test object consisted of two 1 mm inside diameter thin-walled glass capillaries of H_2O attached to the inside wall of a 4.2 mm inside diameter glass tube of D_2O. In the first experiment, both capillaries contained pure water. The proton resonance line width, in the absence of the transverse field gradient, was about 5 Hz.

Assuming uniform signal strength across the region within the transmitter–receiver coil, the signal in the presence of a field gradient represents a one-dimensional projection of the H_2O content of the object, integrated over planes perpendicular to the gradient direction, as a function of the gradient coordinate (Fig. 1). One method of constructing a two-dimensional projected image of the object, as represented by its H_2O content, is to combine several projections, obtained by rotating the object about an axis perpendicular to the gradient direction (or, as in Fig. 1, rotating the gradient about the object), using one of the available methods for reconstruction of objects from their projections[1–5]. Fig. 2 was generated by an algorithm, similar to that of Gordon and Herman[4], applied to four projections, spaced as in Fig. 1, so as to construct a 20×20 image matrix. The representation shown was produced by shading within contours interpolated between the matrix points, and clearly reveals the locations and dimensions of the two columns of H_2O. In the second experiment, one capillary contained pure H_2O, and the other contained a 0.19 mM solution of $MnSO_4$ in H_2O. At low radio-frequency power (about 0.2 mgauss) the two capillaries gave nearly identical images in the
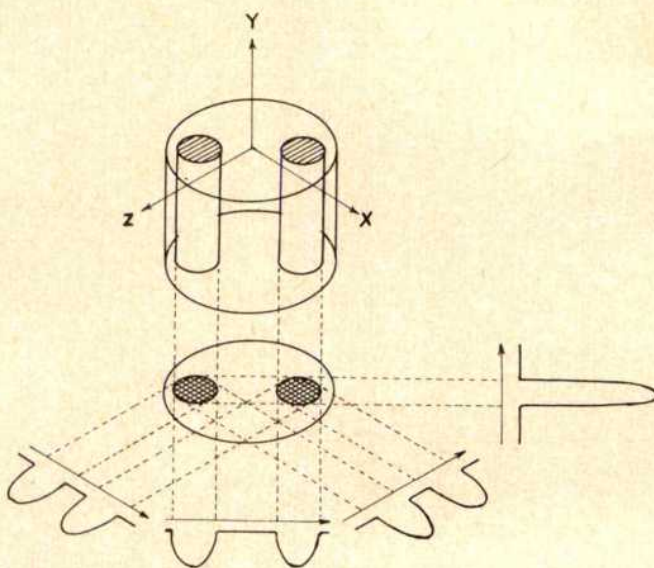
Fig. 1 Relationship between a three-dimensional object, its two-dimensional projection along the Y-axis, and four one-dimensional projections at 45° intervals in the XZ-plane. The arrows indicate the gradient directions.
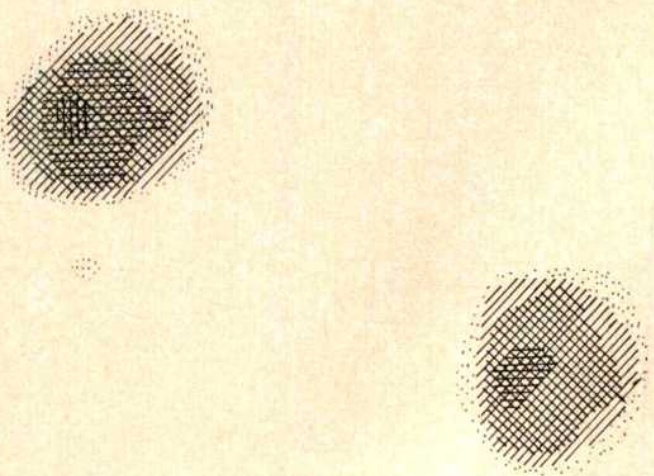
Fig. 2 Proton nuclear magnetic resonance zeugmatogram of the object described in the text, using four relative orientations of object and gradients as diagrammed in Fig. 1.

zeugmatogram (Fig. 3a). At a higher power level (about 1.6 mgauss), the pure water sample gave much more saturated signals than the sample whose spin-lattice relaxation time T_1 had been shortened by the addition of the paramagnetic Mn^{2+} ions, and its zeugmatographic image vanished at the contour level used in Fig. 3b. The sample region with long T_1 may be selectively emphasized (Fig. 3c) by constructing a difference zeugmatogram from those taken at different radio-frequency powers.

Applications of this technique to the study of various inhomogeneous objects, not necessarily restricted in size to those commonly studied by magnetic resonance spectroscopy, may be anticipated. The experiments outlined above demonstrate the ability of the technique to generate pictures of the distributions of stable isotopes, such as H and D, within an object. In the second experiment, relative intensities in an image were made to depend upon relative nuclear relaxation times. The variations in water contents and proton relaxation times among biological tissues should permit the generation, with field gradients large compared to internal magnetic inhomogeneities, of useful zeugmatographic images from the rather sharp water resonances of organisms, selectively picturing the various soft structures and tissues. A possible application of considerable interest at this time would be to the *in vivo* study of malignant tumours, which have been shown to give proton nuclear magnetic resonance signals with much longer water spin-lattice relaxation times than those in the corresponding normal tissues[6].

The basic zeugmatographic principle may be employed in many different ways, using a scanning technique, as described above, or transient methods. Variations on the experiment, to be described later, permit the generation of two- or three-dimensional images displaying chemical compositions, diffusion coefficients and other properties of objects measurable by spectroscopic techniques. Although applications employing nuclear magnetic resonance in liquid or liquid-like systems are simple and attractive because of the ease with which field gradients large enough to shift the narrow resonances by many

line widths may be generated, NMR zeugmatography of solids, electron spin resonance zeugmatography, and analogous experiments in other regions of the spectrum should also be possible. Zeugmatographic techniques should find many useful applications in studies of the internal structures, states, and compositions of microscopic objects.

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BIOLOGICAL SCIENCES

Island Lizards: the Genetic-Phenetic Variation Correlation

NATURAL populations of many organisms are known to contain much more genetic variation than would have been predicted by all but a minority[1] of geneticists two decades ago. Individuals of several species have up to 22% of their loci heterozygous, and from 0–50% or more of the loci in a population are polymorphic, although the higher estimates may result from sampling error[2–4]; vertebrates tend to be at the lower end of these ranges. Estimates such as these are based on electrophoretically detectable variation in proteins, so the true levels of genetic variation are probably higher[5]. These generalizations are gaining wide acceptance, but there is still some unease about their accuracy. The fundamental question is whether the loci being sampled are representative of the genome as a whole. We here present evidence that the electrophoretic approach is relatively unbiased.

Two groups of lizards were used: eight species of *Anolis* from the West Indies and thirteen populations of the side-blotched lizards *Uta stansburiana, sensu latu,* from California and Mexico, caught in 1971 and 1972. Geographic variation is not a source of heterogeneity, as all specimens from a locality were collected within a few hundred metres of one another. After capture, they were transported alive or on dry ice to the laboratory and stored at $-76°$ C until needed. After skinning, water-soluble proteins were routinely extracted and electrophoresed[6]. Six of the eight *Anolis* species were from Puerto Rico, and two, *A. extremus* and *A. roquet,* were from Barbados and Martinique, respectively.

A single morphological character was used to estimate morphological variation in the *Anolis* species; the number of subdigital scales on the longest toe (second) on the hind foot, starting with the most distal lamella and counting proximally. Variability in this character is correlated with variability in other scale characters, but the other characters were not scored as accurately. Estimates of genetic variation in the *Anolis* species were derived from the starch-gel electrophoresis patterns of enzymes and nonenzymatic proteins, which together appear to represent the gene products of twenty-one or twenty-two loci. The proteins assayed were lactate dehydrogenases, malate dehydrogenases, α-glycerol-phosphate dehydrogenase, isocitrate dehydrogenases, indophenol oxidase, phosphoglucose isomerase, phosphoglutamase, glutamic oxaloacetate
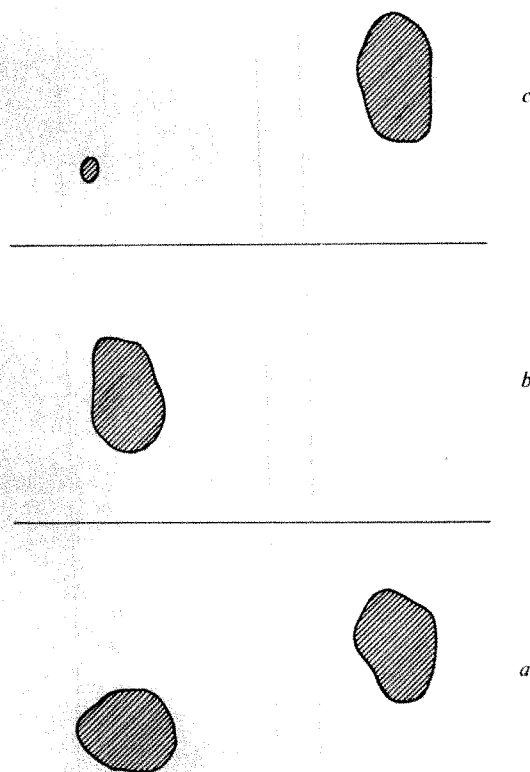
Fig. 3 Proton nuclear magnetic resonance zeugmatograms of an object containing regions with different relaxation times. a, Low power; b, high power; c, difference between a and b.
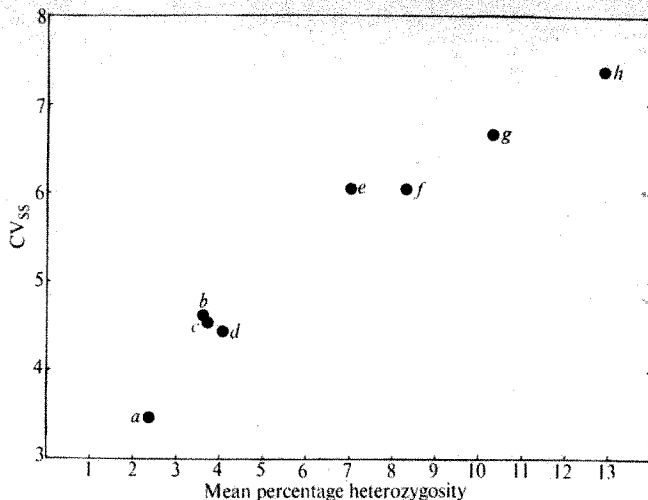
Fig. 1 The association in eight species of *Anolis* of the coefficient of variation of subdigital scales (CV_{ss}) and mean percentage of loci for which an individual was found to be heterozygous in a population. *a*, *A. stratulus*; *b*, *A. poncensis*; *c*, *A. extremus*; *d*, *A. roquet*; *e*, *A. evermanni*; *f*, *A. gundlachi*; *g*, *A. krugi*; *h*, *A. pulchellus*. Sample sizes range between 21 and 30.

transaminases, 6-phosphogluconic dehydrogenase, 4 general proteins, fumarase, peptidase, xanthine dehydrogenase and, except in *A. roquet*, alcohol dehydrogenase. Esterases were excluded because of difficulty in their interpretation.

Five external characters were the basis for estimates of morphological variation in *Uta*. The characters, as described elsewhere[7], include mid-dorsal scales (24), right circumorbitals (28), right supraoculars (31), right femoral pores (34), and scale organs (42) on 31. Except for characters 28 and 31, none are significantly correlated. We used the mean of the five coefficients of variation[8] to estimate overall morphological variation in a population. Estimates of genetic variation were derived from the starch-gel electrophoresis patterns of ten enzymes and four nonenzymatic proteins, which together seem to represent the gene products of nineteen loci. The proteins were the same as with *Anolis* with the following exceptions: two esterases were scored but fumarase, peptidase, xanthine dehydrogenase and alcohol dehydrogenase were not screened.

A priori, the two kinds of variation afford different views of the genome. The morphological data probably provide information on variation over a relatively large fraction of the genome, but environmental heterogeneity may also contribute significantly to the variances of these characters. The electrophoretic data, on the other hand, provide information on a very small fraction of the genome, but this information is virtually free of nongenetic effects. Significant correlation between these two operationally independent estimates would support the hypothesis that both are accurately estimating the same thing—overall genetic variation. It would then follow that a sample of loci as small as twenty or twenty-five can give a reliable estimate of genetic variation in a population. On the other hand, such a correlation does not necessarily imply any overlap in the genetic bases of the morphological and protein characters.

Fig. 1 shows the relation between the two presumed estimates of genetic variation among the eight *Anolis* species. The statistical significance of the association is obvious. Three species available to us were not included because sexual dimorphism in the scale count artificially inflated the coefficient of variation, and the samples were too small to segregate by sex.

Fig. 2 shows the same relation among the *Uta* populations. The pattern of association demonstrates a significant correlation (Spearman rank correlation is 0.60, $P < 0.05$) when considering only populations on the more isolated islands beyond the 100 m depth contour. Most of these deep-water populations

are phenetically distinct and have probably been in continuous existence since before the last glacial maximum[9]. In general, the populations on the mainland and on near-shore, shallow water islands do not conform to the above pattern, being more variable morphologically for a given level of estimated protein variability. We do not know why this is, but one possibility is that these populations have large environmental contributions to their variances compared to the deep-water populations.

Elsewhere[8] (and in preparation), we discuss the separate question of the possible genetic and ecological causes of the different levels of genetic–phenetic variation on islands.

Marshall and Allard[10] have shown a correlation in variation between two sets of Mendelian characters in grasses of the genus *Avena*; one set was electrophoretic, the other was morphological. Our results extend the correlation to continuously varying, obviously polygenic characters. We believe that the available evidence supports the hypothesis that the enzymes and other structural proteins that we and others are using to estimate genetic variation are, in fact, a representative sample of gene products. Our data, however, also suggest that other factors, perhaps environmental heterogeneity, may be a very important source of variation in some morphological characters. In this regard, the correlation in Fig. 1 is somewhat higher than anticipated. It can easily be shown that estimates of heterozygosity based on only twenty loci have appreciable standard errors, so it is likely that further studies will produce results more like those in Fig. 2.
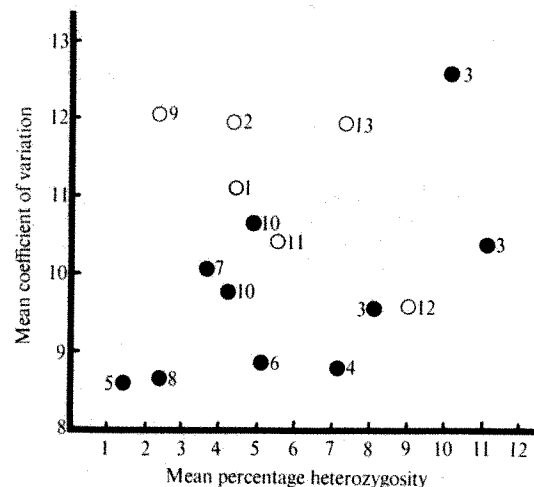
Fig. 2 The association in *Uta stansburiana* of morphological variation, $\bar{V}$ (see text), and average (=mean) % of loci for which an individual was found to be heterozygous in a population. The numbers refer to the following localities: 1, UCSD campus; 2, Punta Bunda, Baja California; 3, three sites on Angel de la Guarda Island; 4, Partida Norte Island; 5, Salsipuedes Island; 6, North San Lorenzo Island; 7, South San Lorenzo Island; 8, San Pedro Martir Island; 9, San Ildefonso Island; 10, two sites on Carmen Island; 11, San Jose Island; 12, San Francisco Island; 13, Espiritu Santo Island. Sample sizes range between 18 and 35. Open circles signify shallow water and mainland populations.

Also, we conclude that, if general heterozygosity is an important source of the differences in morphological variability among the populations, then the assumption that electrophoretically detected allozymes are of no selective significance[11,12] is weakened unless, of course, it is assumed that morphological variation has no selective significance. Several articles indicate that stabilizing selection, at least, affects morphological variation[13–15].

We have considered alternative explanations of the observed correlations. Perhaps the most reasonable is that local environmental diversity determines both genetic variability and morphological variability, but by separate paths. The

available data do not support this conclusion[8], but genetic studies will be required to rule it out altogether.

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Relationship of Enzyme Polymorphism to Species Diversity

SUCCESSFUL adaption by a species to a particular portion of diverse environment depends not only upon the physical characteristics of that environment, but also upon the reliability with which a particular set of characteristics is encountered. A high degree of specialization might be more advantageous when environmental factors occur predictably than when they do not.

Slobodkin and Sanders[1] have suggested that regions of high species diversity tend to be characterized by high environmental predictability. A similar hypothesis was advanced by Connell and Orias[2]. Little unambiguous empirical evidence exists on this point. Hessler and Sanders[3] have shown that deep oceans have high species diversity compared with estuaries, which is consistent with this hypothesis.

A second hypothesis concerns amounts of genetic variation. Species occupying niches, the characteristics of which are highly predictable, might be expected to maintain a lesser degree of genetic variation than species occupying less reliable niches, while situations of low environmental predictability might tend to promote polymorphic gene variation[4,5]. Again, this point has not been empirically demonstrated.

These two untested hypotheses, both phrased in terms of environmental predictability, imply that environments of high predictability may be accompanied not only by high species diversity but also by low degrees of polymorphic gene variation. Thus the two hypotheses are compatible only if levels of species diversity are inversely related to the extent of polymorphic gene variation.

There are few data on which to base a comparison of species diversity and gene polymorphism. The recently reported study on enzyme polymorphism in the Hawaiian *Drosophila* by Rockwood *et al.*[6] does permit such a comparison, although it must be considered preliminary (the data involve the use of but one standard, interspecific homologies are uncertain, and the sample sizes are often small, particularly from Kaui where some species are represented by single individuals).

The levels of *Drosophila* species diversity on each of the Hawaiian Islands, and the evolutionary relationships between these species, are well documented (for a review see Carson[7]). I here express the levels of *Drosophila* species diversity on each island in terms of the total number of *Drosophila* species per island; species diversity may also be expressed solely in terms of the "picture wing" species (Maui=30, Hawaii=17, Oahu=11, Kauai=9). Following other authors, I treat the islands of Maui, Molokai, and Lanai as a single evolutionary unit (the three islands have been fused into a single above-water land mass at least twice, and are in close proximity).

To estimate the level of allozyme diversity characteristic of each island, I have utilized the Rockwood data on patterns of enzyme polymorphic variation at six enzyme loci among fifty-one "picture wing" species of Hawaiian *Drosophila*. This estimation involves several assumptions which must be carefully examined. (*a*) It assumes that the selection of species examined is representative of the total number of species. The almost exclusively island-endemic "picture wing" species group of Hawaiian *Drosophila* is distributed in a manner similar to that of the total number of *Drosophila* species (15 to 20% of all species are members of the picture wing group on each of the islands). (*b*) It assumes that the number of allelic forms observed in the sample is representative of the species, rather than reflecting the character of a local population. In the few species in which the effect of geographic isolation has been examined, differences are chiefly in gene frequency rather than in the total number of allelic forms observed. (*c*) It assumes an unbiased selection of alleles. All populations considered must be analysed for the same assortment of loci, as some loci will exhibit far more diversity than others. Among the fifty-one picture wing species, thirty-eight species were analysed at all six loci, nine species at five loci, and one species at four loci; the remaining three species were analysed at fewer loci, and were not considered in my analysis.

I have expressed levels of allozyme diversity as the ratio of the number of different allozyme types observed to the number of species examined. Similar results are obtained if allozyme diversity is expressed as $(\Sigma\, n \log n)/$(the number of species examined), where n=the proportion of observed species in which a given allele occurs.

Comparing the estimates of allozyme and species diversity described above, it is clear that an inverse relationship exists (Fig. 1). Similar results are obtained when information theory measures of allozyme diversity are used, or when species diversity is characterized solely in terms of the picture wing species.

These levels of allozyme diversity do not correlate with obvious physical and genetic factors, such as: (1) the age of the islands (Kauai is the oldest, Hawaii the youngest); (2) the area of the island (Kauai is the smallest, Hawaii the largest); (3) the distances between them; (4) estimates of evolutionary distance (the chromosomal relationships among the Hawaiian *Drosophila* are known in detail[7]; among the picture wing species, assuming the ancestral form to be *D. primaeva*, no significant regression exists for allozyme diversity as a function of the number of inversion differences from ancestral form); (5) founder effects (chromosomal relationships indicate that the minimum number of inter-island founders in the picture wing species is one for Kauai, six for Oahu, six for Maui, and nine for Hawaii); (6) sample size (the small samples are from Kauai, which shows the
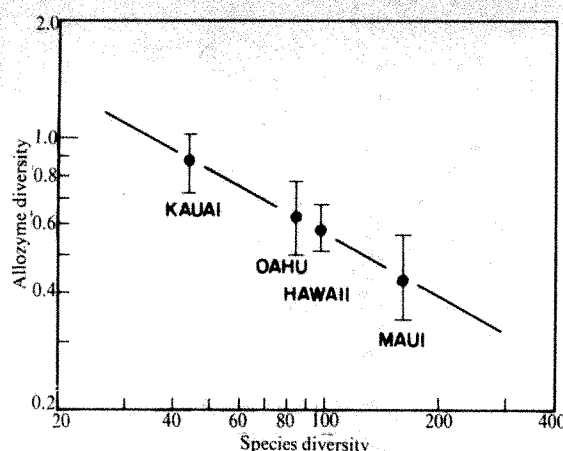
Fig. 1 The relation of allozyme diversity to species diversity in Hawaiian *Drosophila*. Allozyme diversity is expressed as the number of different allozyme types of an enzyme observed on an island divided by the number of species examined on that island. The allozyme data used are those of Rockwood *et al.*[6]. Species diversity is expressed as the total number of *Drosophila* species found on a given island. Mean values for the six enzyme loci are presented, with standard error indicated. A linear plot is also highly significant. A linear regression (calculated using UCIA Biomed. Multiple Regression Program) yields a regression coefficient of -0.004; $F_{1,22}=6.68$, $0.01 < P < 0.025$, indicating a high level of significance.

greatest diversity; increasing these sample sizes could not reduce the number of allozyme types seen); (7) total number of allozyme types (the greatest number of different types are seen on Maui, the least on Kauai).

A further technical point must be considered. As interspecific homologies are not certain in the Rockwood study, it is important to estimate the extent to which possible errors in allele assignment might affect the significance of the allozyme diversity estimates of Fig. 1. Such mistaken assignments would occur most frequently between alleles of similar mobility. Thus errors in allele assignment should reflect the frequency distribution of the allele mobility types on the various islands. In the Rockwood study, the shapes of the allele distribution curves are very similar for a given locus from island to island. For the four islands, mean values for "evenness"[8] of allele distributions are 0.46, 0.51, 0.53, and 0.49, indicating that the relative information content of the allele distributions is quite similar on the four islands. Thus errors in allele assignment should not affect the significance of the relationship seen in Fig. 1.

The inverse relationship observed between species diversity and enzyme polymorphism diversity is that which would be expected if both parameters were influenced by environmental predictability, as current hypotheses suggest. As detailed knowledge of the ecology of specific species becomes available, and more complete survey data are obtained on the relevant allozymes, it may become possible to relate niche breadth with respect to a particular resource to the levels of allozyme diversity at loci concerned with utilization of that resource. Until such data are available, however, it should be kept clearly in mind that measures of diversity which average over a variety of enzymes or over ecologically diverse species are at best only an indication of more complex underlying processes.

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Carcino-Foetal Human Liver Ferritins

FERRITIN is an iron-storage protein found in the cytoplasm of a wide variety of plant and animal cells[1,2]. Structurally, the molecule comprises a hollow protein shell, apoferritin, composed of 20 or 24 subunits, within which variable amounts of inorganic iron may be sequestered. These subunits may not be chemically identical since multiple molecular forms of differing charge, isoferritins, have been found in several organs by electrophoresis[3,4] or electrofocusing[5,6]. Although the structural relationship of the isoferritins is unclear, these findings raise the possibility that the charge differences may represent primary structures coded by different genes. In addition to the isoferritins found in normal cells, an "abnormal" ferritin has also been found in malignant cell lines[7] and in livers of tumour bearing animals[8,9]. As part of our investigations into tumour specific and embryonic antigens, we have examined the isoferritin profile in human hepatoma and compared it to that found in normal adult and foetal liver. Here we supply evidence for a unique isoferritin species in human hepatoma that is not present in normal adult liver. This tumour-specific isoferritin may correspond to a similar isoferritin found in foetal liver in early gestation.

Ferritin was isolated from normal human livers, foetal livers at various stages of gestation and from human hepatoma tissue by the method of Drysdale and Munro[10]. A chromatographic step on CM-cellulose was omitted to prevent possible loss of isoferritins of differing charge. Tissues were blotted dry of residual blood, homogenized in 4 volumes of water, then heated to 75° F for 2 min to precipitate heat labile proteins. The supernatant fraction was adjusted to pH 4.6 to remove other contaminants and ferritin was subsequently recovered from the supernatant and precipitated in 33% ammonium sulphate. The pellet was dissolved in 0.02 M KH_2PO_4, chromatographed on 'Sephadex G-200' and eluted in the void volume. These preparations contained only ferritin and its higher polymeric forms when examined by polyacrylamide gel electrophoresis.

Table 1 pI of Human Liver Ferritins

Peak	Normal	Foetal	Hepatoma
1	5.55		
2	5.50		
3	5.45 *	5.45	5.47
4	5.33	5.34 *	5.36
5	5.29	5.28	5.29 *
6		5.22	5.23 *
7			5.15

* The principal molecular form.

As a further purification, some of these preparations were subjected to isoelectric focusing in a 110 ml. sucrose density gradient containing 4% (w/v) 4–6 or 5–7 'Ampholines' (LKB Produkter, Sweden[11]). After 3–5 days electrolysis, 0.5 ml. fractions were collected from the bottom of the column, and the pH gradient measured with a microelectrode. Apoferritin

was identified and quantitated by electroimmunodiffusion[12] using monospecific rabbit anti-human liver ferritin.

All preparations resolved into multiple components on isoelectric focusing, with at least six or seven distinguishable peaks. The pIs of the isoferritin peaks in hepatoma, adult and foetal liver are given in Table 1. The principal peak in normal adult liver was isoelectric at pH 5.45 with several minor components between pH 5.3 and 5.5. The foetal and hepatoma isoferritin profiles showed the same components, but in both cases the more acidic components predominated. In addition to these common components, the hepatoma ferritin contained a more acidic form, pI 5.1, that was not demonstrated in normal liver.

To examine these profiles in more detail, the purified ferritin preparations were subjected to gel electrofocusing[13] (Fig. 1). Normal ferritin consistently showed at least three major bands. The hepatoma isoferritins contained at least one of these three components, but in addition demonstrated a molecular form with a lower pI that is not present in normal ferritin. This tumour-specific isoferritin was also apparent in early foetal ferritins, 12–20 weeks of gestation, which contained bands common to both hepatoma and normal ferritin with a variable pattern. The oldest foetus (35 weeks of gestation) had an isoferritin pattern that was indistinguishable from normal, adult ferritin.
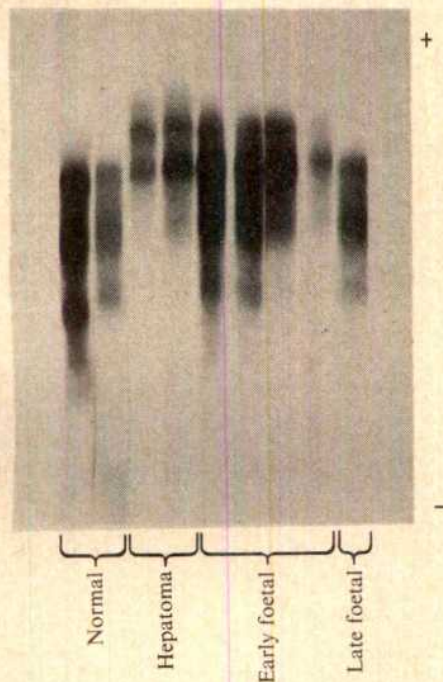
Fig. 1 Analytic isoelectric focusing in 4% polyacrylamide gels using 2% ampholyte pH range 4–6. Ferritin isolated from two normal, two hepatoma and five foetal livers was applied. After equilibrium was attained, the gels were stained for iron with Prussian blue. Similar patterns were obtained by using protein stains.

In order to confirm that these multiple forms of ferritin represented distinct molecular species, the isoferritins were separated and re-examined. The acidic, central and basic isoferritin fractions from hepatoma ferritin were separated by preparative isoelectric focusing in sucrose. The portions were dialysed against 0.02 M phosphate buffer pH 7.4 and concentrated by vacuum dialysis. The concentrated pools were then refocused on the analytical 4% polyacrylamide gels as previously described and stained for iron with Prussian blue (see Fig. 2). The different molecular forms of hepatoma ferritin did not redistribute, but refocused to the same position. The isoferritin isolated with the most acid pI was not present in normal ferritin, suggesting the presence of a chemically unique hepa-
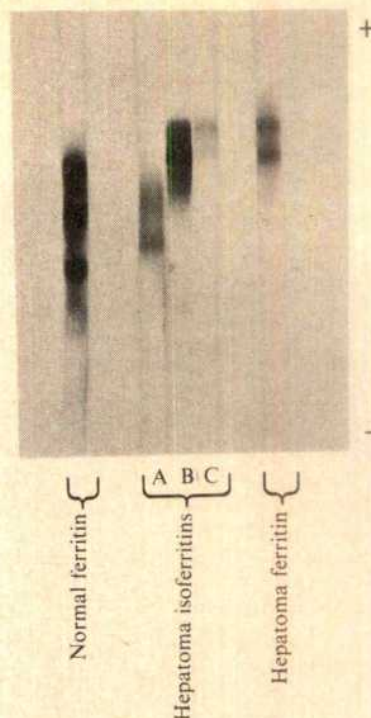
Fig. 2 Hepatoma isoferritins were separated by preparative isoelectric focusing into a basic pool (A), pI 5.32–5.80, the main peak (B), pI 5.20–5.30, and the most acidic forms (C), pI 4.74–5.18. These pools were dialysed against 0.02 M phosphate buffer (pH 7.4), concentrated, and aliquots applied to analytic isoelectric focusing in 4% polyacrylamide gels, ampholyte pH 4–6. After equilibrium was attained, the gels were fixed and stained for iron by Prussian blue.

toma ferritin form. The structural relationships of the isoferritins revealed by isoelectric focusing have not yet been resolved. The heterogeneity is not due to difference in iron content or aggregate size and appears to represent charge differences either from different primary structure or post-synthetic modification of one or more of the subunits. The appearance of a unique hepatoma isoferritin suggests that the tumour not only synthesizes at least some of the components found in normal ferritin, but may make a unique tumour-specific or carcino-foetal ferritin subunit. The biochemical structure of these ferritin forms and their subunit structure are under further investigation.

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The Effect of Mutation on Population Size

AFTER the work of Haldane[1] and Muller[2], much has been written about the genetic load caused by mutation. This mutational load had been defined as the fraction by which the mean fitness of a population subject to mutation differs from the fitness of the wild (non-mutant) genotype[3]. The operational definition of load is then

$$L = \frac{W_{max} - \overline{W}}{W_{max}} \qquad (1)$$

where W_{max} is the fitness of the non-mutant genotype, and $\overline{W}$ the mean fitness of the population subject to mutation.

Some workers have supposed, implicitly or explicitly, that the average selective value is necessarily an indicator of the relative fitness or competitive ability of a population compared to other populations. This supposition is incorrect because it is based on an extrapolation of measures of relative fitness within populations (selective values) to comparisons between populations[4,5]. Further confusion has been caused by the assumption that the genetic load is a measure of factors directly related to population size[6]. Here I report some results from a study of the effects of mutation on population numbers, using earlier work on density-dependent selection[7-11] to bridge the gap between the theories of ecology and population genetics.

The proportional reduction of numbers brought about by mutation (the numerical load) for populations that are in numerical equilibrium can be defined in an analogous way to the definition of the conventional genetic load.

$$NL = \frac{\hat{N}_0 - \hat{N}_{mut}}{\hat{N}_0}$$

where $\hat{N}_0$ is the numerical equilibrium in the absence of mutation, and $\hat{N}_{mut}$ is the equilibrium in its presence[11].

Assuming a large random-mating population with discrete generations and without immigration or emigration, let us suppose that there are two alleles M and m at an autosomal locus, and that M is completely dominant to m. The frequency of M among the adults of one generation is p, and the frequency of m is q $(p+q=1)$. M is the "wild-type" gene and m is the mutant. The mutation rate from M to m is μ. When m is rare we can ignore back-mutation from m to M. If mutation occurs during the formation of gametes and if all three genotypes have equal fertility, the gene frequency of m among the gametes will be

$$q' = q + \mu (1-q)$$

When the phenotypes have different probabilities of surviving to produce offspring, represented by the selective values a (for M–) and c (for mm), the phenotype frequencies after selection will be

Phenotype	M–	mm
frequencies after selection	$a(1-q'^2)$	cq'^2

and the overall change of gene frequency will be

$$\Delta q = \frac{(1-q')\,[q'^2\,(c-a)+a\mu]}{(1-\mu)\,[q'^2\,(c-a)+a]} \qquad (2)$$

When there is a balance between mutation and selection, Δq is zero and

$$\hat{q}' = \sqrt{\frac{a\mu}{a-c}}$$

where $\hat{q}'$ is the non-trivial equilibrium value of q'.

From equation (1) the genetic load at equilibrium is

$$L = \frac{a-[q'^2\,(c-a)+a]}{a} = \mu \qquad (3)$$

The selective values (a and c) are conventionally defined as measures only of relative fitness. The equations given above, however, are equally valid if a and c are absolute fitnesses. In this event they measure changes in the numbers of each genotype from generation to generation. The average selective value ($\overline{W} = q'^2\,(c-a)+a$) is then related to the overall change in numbers (ΔN) by

$$\Delta N = N\,(\overline{W}-1) \qquad (4)$$

where N is the total number of adult organisms in the population.

When the population is at equilibrium for both numbers and gene frequency, $\Delta q=0$ and $\Delta N=0$. Then, from equations (2) and (4),

$$a = \frac{1}{1-\mu} \qquad (5)$$

$$c = \frac{\hat{q}'^2 - \mu}{\hat{q}'^2\,(1-\mu)} \qquad (6)$$

These equations are general, and can be applied whether the selective values are constant or variable. If the selective values are functions of population size, equations (5) and (6) can be used to derive the value of N at equilibrium. Thus we can solve $\hat{N}$ as well as $\hat{q}'$. The precise result will depend upon the form of the relation between selective value and population size.

Following an earlier study[11], this relation is assumed to be

$$a = \frac{w_1 k_1}{k_1 + w_1 N\,(1-q'^2) + \alpha_1 w_2 N q'^2} \qquad (7)$$

$$c = \frac{w_2 k_2}{k_2 + w_2 N q'^2 + \alpha_2 w_1 N\,(1-q'^2)} \qquad (8)$$

where w_1 and w_2 represent the "intrinsic selective values" (density-independent rates of increase, including the effects of density-independent mortality, which is assumed to act first), k_1 and k_2 measure the "carrying capacity" of the environment for each genotype, and α_1 and α_2 are coefficients of competition.

A consideration of a and c makes it clear that a mutant could be disadvantageous in three different ways. It could have a reduced intrinsic selective value (w), a reduced carrying capacity (k), or a reduced competitive ability (either an increased value of α_2 or a reduced value of α_1).

These three situations can be considered separately. If the mutant has a reduced intrinsic selective value, we can assume $w_1 = w$, $w_2 = w\,(1-s)$. $k_1 = k_2$, $\alpha_1 = \alpha_2 = 1$ (note that if α_1 and α_2 are less than one the system may become a balanced polymorphism[11]). Substituting in equations (7), (8), (5), (6) and (2) we find the numerical load

$$NL_{(w)} = \frac{\mu}{(w-1)\,(1-\mu)} \qquad (9)$$

Similarly, the numerical load for a mutant reducing the carrying capacity (if $k_1 = k$, $k_2 = k(1-s)$, $w_1 = w_2$, $\alpha_1 = \alpha_2 = 1$) is

$$NL_{(k)} = \frac{w\mu}{w-1} \qquad (10)$$

When mutation increases α_2 (that is, when $\alpha_1 = 1$, $\alpha_2 = 1+s$)

$$NL_{(\alpha_2)} = \frac{w\mu}{w-1} \text{ as before} \qquad (11)$$

but when it decreases α_1 (that is, when $\alpha_1 = 1-s$, $\alpha_2 = 1$)

$$NL_{(\alpha_1)} \cong \frac{w - \sqrt{s\mu w(w-1)}}{w - 1 - \sqrt{s\mu w(w-1)}} \qquad (12)$$

which is negative if $s > \mu$ (that is, when there is a balance between mutation and selection). Details of the approximation are given elsewhere[12].

If the density-dependent component of selection is assumed to act before the density-independent component, the numerical loads are unchanged, except that the w load becomes

$$\frac{w\mu}{(w-1)(1-\mu)}$$

like the k and α_2 loads.

Several conclusions emerge. First, it is possible to combine the theoretical assumptions of ecology and population genetics, and to predict the effects of mutation on equilibrium population size. Second, although all disadvantageous mutants produce the same genetic load (as conventionally defined), different types of mutants may have different effects on the numerical equilibrium. Third, in relation to their effects on population size, disadvantageous mutants can be grouped into three broad classes, which are not mutually exclusive; w-mutants, with reduced density-independent selective value (and consequently a reduced intrinsic rate of increase), k-mutants, with a reduced carrying capacity, and α-mutants with a reduced competitive ability. Selection against α-mutants probably corresponds to the "soft selection" of Wallace[6]. Fourth (perhaps the most surprising conclusion), in some circumstances the presence of disadvantageous mutants can cause an increase in population size, despite the fact that the mutants are eliminated by natural selection.

Studies using other ecological models, including the logistic conclusion, suggest that these conclusions are general (see ref. 12 and L. Nunney, personal communication). It is quite clear that in order fully to understand the consequences of mutation we must take into account its effects on the ecological parameters of populations.

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Effect of Hyperbaric Oxygen on Cultured Foetal Hearts

FOETAL mouse hearts and foetal hearts from other species have been shown to have remarkably consistent performance in organ culture. Wildenthal[1,2] demonstrated that various substances added to an organ culture medium prolonged the survival of foetal hearts, and Hughes and Longmore[3] showed that survival time and beating were related to the stage of development of the embryo, the younger hearts living and beating longer and better than the older hearts. Longmore and Hughes[4] have shown that there is no difference in the performances of composite hearts made from parts of foetal hearts of different species at the same stage of maturity. It has been suggested by Wildenthal (personal communication) that the effect of substances on the heart may be different before and after the nerve end plates have developed.

All the culture techniques used 95% oxygen and 5% CO_2 at 1 atm but New[5] has shown that hyperbaric oxygen, at 2 to 3 atm, permits prolonged survival of twenty-five somite rat embryos in static culture medium and forty somite rat embryos in circulating medium. The inference was that hyperbaric oxygen might improve the performance of standard foetal heart cultures. From our clinical experience on the effects of hyperbaric oxygen we doubted whether oxygen at above normal pressures would have anything but harmful effects. To establish whether this was so, we set out to culture, in our standard medium, control hearts and hearts set up in a simple hyperbaric chamber.

Litters of mice, 11 and 16 days of gestation, were used. Half of each group were used as controls and half were subjected
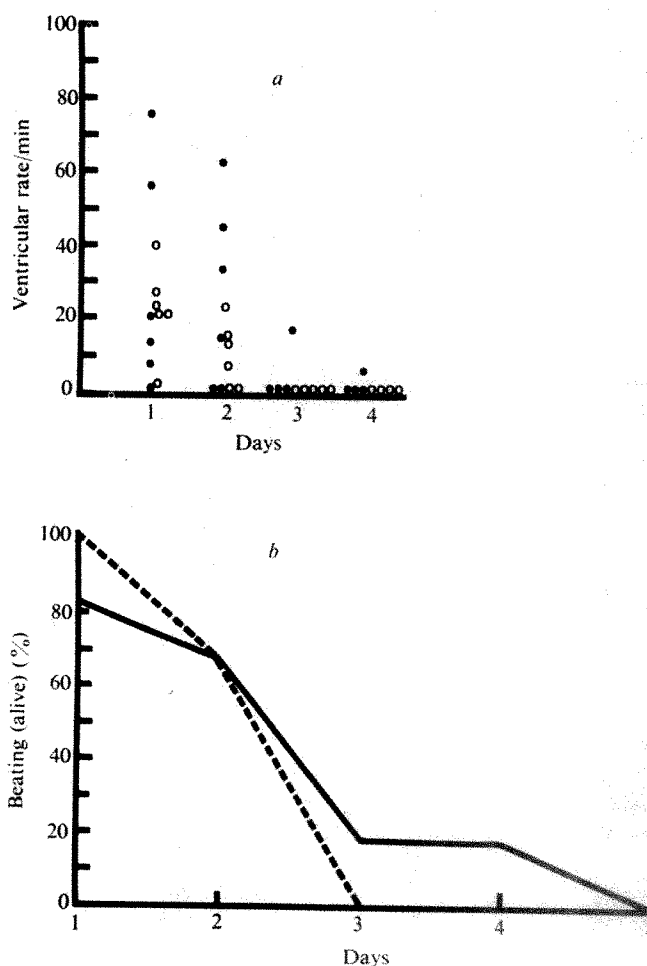
Fig. 1 Eleven-day-old foetal hearts (before innervation). a, Beating performance. ●, Control; ○, hyperbaric. b, Survival. ——, Control; - - -, hyperbaric.
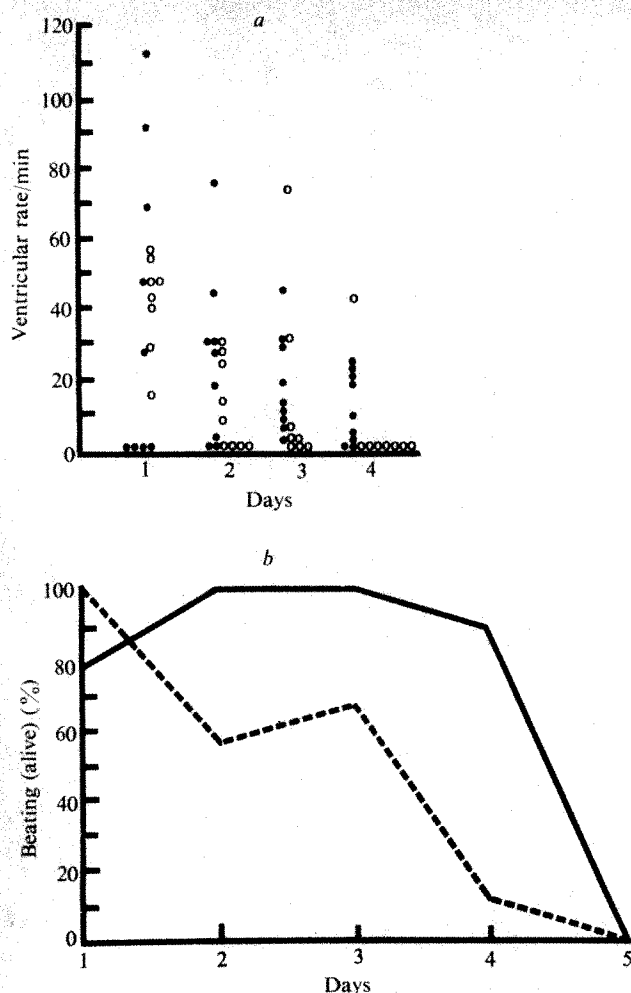
Fig. 2 Sixteen-day-old foetal hearts (after innervation). a, Beating performance. ●, Control; ○, hyperbaric. b, Survival. ——, Control; - - -, hyperbaric.

to hyperbaric oxygen. During dissection the atria were left intact whenever possible. The hearts were placed on stainless steel wire mesh grids and arranged so that just the bottom surface of the hearts was in direct contact with the medium. Burroughs Wellcome 199 culture medium, with 35% colostrum deprived calf serum, plus 50 mg ml.$^{-1}$ insulin and 0.1 µg ml.$^{-1}$ cortisol, was used as the culture medium.

A special chamber was constructed for the hyperbaric cultures in order to maintain and withstand the increased pressure. Inlet and outlet valves, as well as a pressure gauge, were added to regulate the pressure to precisely two atmospheres. The culturing technique was exactly as for the controls except for the increased P_{O_2}. The P_{CO_2} remained at 38 mm mercury for both groups while the P_{O_2} was increased from 722 mm of mercury to 1,482 mm of mercury in the hyperbaric groups.

Both the control hearts and those in the hyperbaric chamber were examined daily to check rate and strength of contractions. The medium was changed every second day. Hearts were considered to be living as long as there was any sign of contraction. For the hyperbaric group approximately 15 min was allowed for decompression before examination to prevent any remote possibility of dissolved oxygen coming out of solution as destructive bubbles.

In all the experiments, which were satisfactory from the technical point of view, the control hearts lived longer and beat faster than the hearts which were subjected to hyperbaric oxygen (Figs. 1 and 2). An anomaly has been that although the hyperbaric hearts beat more slowly and died sooner than the controls, the strength of their contraction was observed to be greater during the short time that they lived. The total

number of these stronger beats was reduced by merit of their shorter survival and of their slower rate.

The detrimental effect of hyperbaric oxygen can probably be related to the small size of the cultured organs and the fact that they rested on the surface of the medium rather than being immersed in it. Hearts cultured and used for the evaluation of drugs should therefore not be cultured in hyperbaric oxygen.

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The Effect of Fatty Acids on the Binding of Tryptophan to Plasma Protein

THE amino-acid tryptophan has a special role as a precursor of the putative transmitter 5-hydroxytryptamine (5HT). Furthermore, in the brain, tryptophan hydroxylase, the rate-limiting enzyme for 5HT synthesis, is normally unsaturated with tryptophan[1,2]. Therefore any mechanism by which brain tryptophan concentration can be altered may conceivably be able to influence brain function.

Food deprivation[3,4] or immobilization stress[4] both lead to increased brain tryptophan and increased turnover of brain 5HT as indicated by raised concentrations of its metabolite 5-hydroxyindolylacetic acid. The increase of brain tryptophan is not simply due to increased plasma tryptophan as these parameters are not significantly correlated[4]. It is, however, associated with an increase of the small fraction of plasma tryptophan which is free[5] (ultrafilterable). Also, a number of drugs which when given to rats increase their brain tryptophan also release protein-bound (non-ultrafilterable) tryptophan from plasma in vitro[6]. These findings point to plasma-free tryptophan as an important determinant of brain 5HT turnover and in turn raise the question of what controls levels of the former.

Not only the plasma-free tryptophan concentration but also that of unesterified fatty acid increases during deprivation[5]. The possibility therefore arises of a causal relationship between these changes. This is also suggested by the finding that oleate interfered "to a minor extent" with the binding of tryptophan to bovine serum albumin, albeit under non-physiological conditions[7]. Plasma unesterified fatty acids are normally almost completely bound to albumin[7,8] while plasma tryptophan is largely bound to albumin[7].

It has now been shown that the addition in vitro of physiologically occurring unesterified fatty acids to rat and human plasma within the range of physiological concentration results in elevation of free tryptophan. Linoleic, oleic and palmitic acids were used. These are the major unesterified fatty acids of human plasma[9] and similar results were obtained on rat plasma when analysed by a gas chromatographic method.

Human and rat blood samples were collected into heparinized tubes, immediately centrifuged and the plasma deep
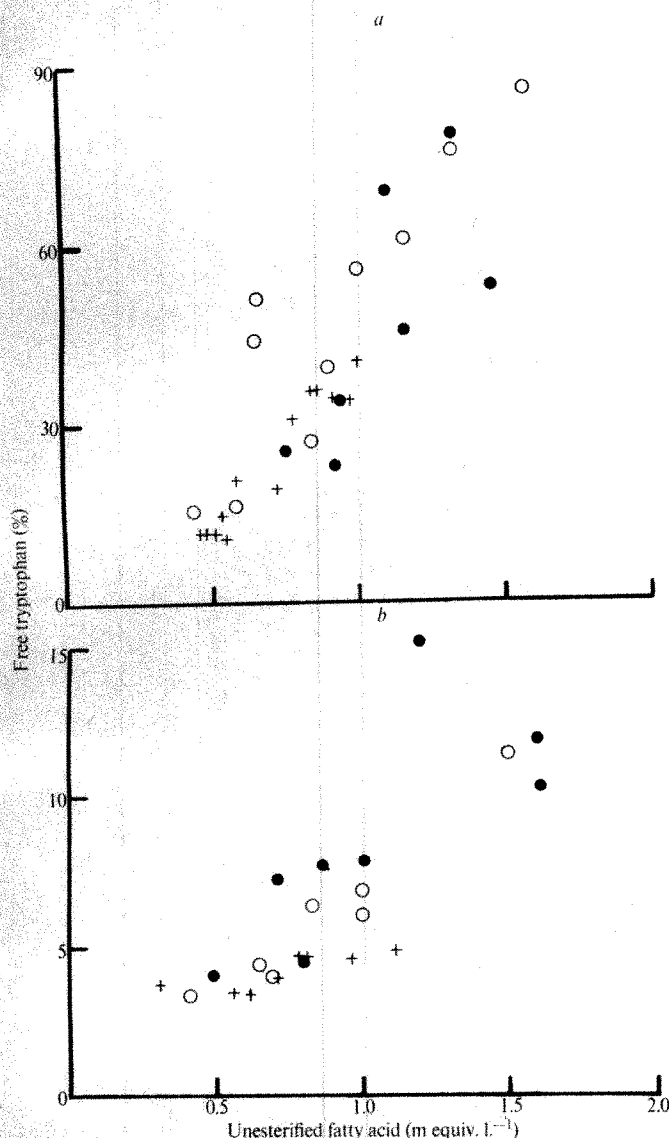
Fig. 1 Effect of *in vitro* addition of unesterified fatty acids to plasma on free (ultrafilterable) tryptophan. *a*, Rat plasma; *b*, human plasma. ○, Linoleic acid; ●, oleic acid; +, palmitic acid. Correlations: free tryptophan versus unesterified fatty acid. Rat: linoleic (10), $r=0.90$, $P<0.001$; oleic (7), $r=0.73$, $P\simeq0.05$; palmitic (13), $r=0.95$, $P<0.001$. Human: linoleic (7), $r=0.97$, $P<0.001$; oleic (8), $r=0.74$, $P<0.05$; palmitic (8), $r=0.79$, $P<0.05$. Number of observations in parentheses. One batch of bulked rat plasma (total tryptophan$=12.1$ µg ml.$^{-1}$) was used with palmitic acid and a second batch (total tryptophan $=16.2$ µg ml.$^{-1}$) with linoleic and oleic acids. A single batch of bulked human plasma was used (total tryptophan$=14.3$ µg ml.$^{-1}$).

frozen, except for 0.05 ml. of each human plasma on which unesterified fatty acid was determined[10]. Human plasmas with fatty acid >0.6 mequiv. l.$^{-1}$ were discarded and the rest bulked. All rat plasmas were bulked. Fatty acids were dissolved in samples of bulked plasmas by a modification of the method of Meinertz[11]. Briefly, 0.25–2.0 ml. of 2.0 mM solutions of the fatty acids in petroleum ether (40°–60° C) were pipetted into 18 mm diameter tubes and made to 2.0 ml. with petroleum ether. The solutions were taken to dryness at 37° C on an 'Evapomix' multiple evaporator. After addition of 2.0 ml. pooled plasma/tube the dried fatty acids were partly dissolved by gentle shaking at 37° C for 1 h, the supernatants were pipetted off and free and bound tryptophan and fatty acid determined on them as previously described[5] (Fig. 1). Increase of free tryptophan correlated significantly with the amount of fatty acid dissolved for all three fatty acids and for both rat and human plasma. Total tryptophan concentrations were comparable for both rat and human plasmas but free tryptophan concentrations in the absence of added fatty acid were considerably greater in rat plasma. An increase of the fatty acid concentration from 0.5 to 1.0 mequiv. l.$^{-1}$ led to four-fold and almost two-fold increases of the free tryptophan concentrations of rat and human plasma respectively. In a subsidiary experiment (not shown in Fig. 1) *in vitro* increase of human plasma palmitic acid to a total unesterified fatty acid concentration of 2.0 mequiv. l.$^{-1}$ led to 50% of the total tryptophan being free.

Previously the best indication that increased plasma unesterified fatty acid led to increased free tryptophan was that, after heparin injection, both were elevated[5]. Heparin releases tissue lipase into the plasma so that plasma glycerides are hydrolysed to unesterified fatty acids[12]. It was conceivable that heparin influenced tryptophan binding by some mechanism involving not fatty acids but increased sympathetic activity[13]. We now find, however, that previous administration of the sympathetic β-blocker propranolol did not prevent the increases of plasma fatty acid or free tryptophan after heparin injection (Table 1). On the contrary, results suggest that propranolol increases the effect of heparin on tryptophan.

Results obtained therefore strongly indicate that plasma fatty acid changes have a role in determining the availability of tryptophan to the brain and hence 5HT turnover therein. They also suggest a mechanism by which the many hormonal agents which alter lipolysis and fatty acid levels through influencing fat cell cyclic AMP[15] might be able to alter brain 5HT turnover. Such a mechanism could be significant in many physiological or pathological circumstances. Also the alteration of fat cell cyclic AMP concentration by drugs might perhaps also lead to altered brain 5HT turnover. Finally, raised plasma unesterified fatty acid concentrations in conditions such as liver disease[16] and migraine related to fasting[17] suggest the possibility of increased brain 5HT turnover in these conditions.

We thank the Medical Research Council and the Research

Table 1 Effect of Heparin and Propranolol on Plasma Total and Free Tryptophan and Plasma Unesterified Fatty Acids

Treatment		Total (µg ml.$^{-1}$)	Tryptophan Free (µg ml.$^{-1}$)	% Free	Unesterified fatty acids (mequiv. l.$^{-1}$)
0 min	30 min				
Saline	Saline	17.68 ± 3.77	$P<0.02$ $\begin{cases}1.69\pm0.51\\2.87\pm0.78\end{cases}$	9.6	$P<0.001$ $\begin{cases}0.20\pm0.07\\0.62\pm0.15\end{cases}$
Saline	Heparin	14.53 ± 3.47		19.9	
Propranolol	Saline	19.32 ± 3.12	$P<0.01$ $\begin{cases}1.94\pm0.42\\6.42\pm2.51\end{cases}$	10.0	$P<0.02$ $\begin{cases}0.27\pm0.15\\0.66\pm0.27\end{cases}$
Propranolol	Heparin	19.55 ± 3.01		32.8	

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Fig. 1 Mouse embryo fibroblasts growing on the strips in the lipid film. *a*, Cells migrated into the strips from the monolayer (× 70). *b*, Autoradiographic preparation of the cells in the strips labelled with ³H-thymidine (1 μCi ml.⁻¹ for 2 h) (× 280).

The Use of Phospholipid Film for Shaping Cell Cultures

It would be useful for many studies of cell–cell interaction (for example, contact inhibition of movement, topoinhibition, electrical coupling) to be able to prepare cell cultures of various defined shapes and sizes. This can be done by protecting the whole surface of the culture substrate, except for desired regions, with a non-adhesive substance. The cells would then adhere and proliferate only in these regions. The protective substance must be (i) non-adhesive for cells; (ii) non-toxic for cells; (iii) insoluble in the media and (iv) strongly attached to the underlying substrate so that neither the size nor shape of adhesive region would change during cultivation. Lieberman et al.[1] used dried agar film on a collagen layer as the non-adhesive substance for cardiac muscle cells.

Our aim was to find a non-adhesive film, suitable for experiments with fibroblasts and other types of cultured cells. A number of substances were tried (paraffin, fatty acids, cholesterol) and found to be unsuitable as they were all more or less adhesive for mouse fibroblasts. The only film which satisfied our requirements outlined above was that prepared from brain phospholipids.

The lipids were extracted from the white matter of calf brain by chloroform–methanol[2,3]. They were dried before use and redissolved in decane or benzene to a concentration of 10 mg ml.⁻¹. To obtain the film, a drop (about 0.02 cm³) of the solution was drawn out of the pipette into the middle of the coverslip, which was rotated horizontally at 2–2,500 r.p.m. This spread the lipids evenly and, after drying, a film was formed strongly attached to the coverslip. A part of this film could be easily removed (mechanically or with a solvent) so that regions of clean glass of any shape could be made. In particular very narrow strips (5–15 μm wide) could be cleaned
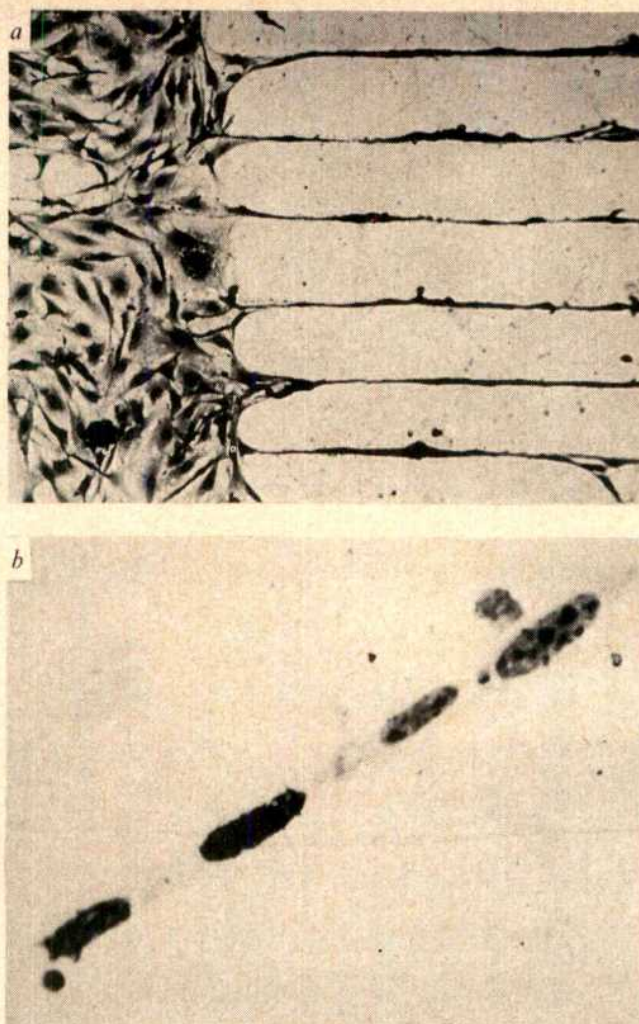
with a blade or with a thin tungsten electrode. The lipid film was found to be firmly attached to the glass: the width of the strips, scratched in the film, did not change after 7 days of incubation in the serum supplied medium, either with the cells or without them.

The following cell types were used: (i) mouse embryo fibroblasts; (ii) the cells of L-strain[4]; (iii) "Chim" strain cells obtained from mouse sarcoma induced by plastic film, and (iv) epithelial kidney cells, transformed with SV40. Cultivation media, the methods of autoradiography and time-lapse microcinematography were similar to those described earlier[5,6].

The cells of all the types used did not spread on the lipid film. As shown by time-lapse cinematography the cells lying on the lipid film retained their spherical form for many hours and continuously formed and withdrew short cytoplasmic processes. These cells remained alive for at least 3 days; they could be reseeded on the glass after that period. When only a part of the glass was covered by the lipid film the cells normally attached themselves to the glass even in the immediate vicinity of the lipid layer. The fibroblasts near the film eventually oriented themselves parallel to its edge. The leading edge of the cell contacting with the edge of the film did not stop undulating, but did not attach to phospholipid. Simultaneously a new leading edge was developed usually in the direction of the border of the film. The cells in contact with the edge of the lipid layer were able to synthesize DNA as well as other cells on the glass; for example, the ³H-thymidine labelled mouse fibroblasts growing for 4 days in narrow

(15 µm wide) strips (Fig. 1) of the glass, surrounded by lipid film had the same labelling index as the control cells on the clean coverslip.

All these experiments confirm that the lipid film was stable, non-adhesive and non-toxic for the culture types used.

By removing a certain part of the lipid film it is possible to obtain the culture of almost any desired shape. In particular, the cells growing on narrow (10 mu wide) strips of the glass may be used for many types of experiments. The cells in these strips formed "monolines", that is, rows of elongated cells (Fig. 1b). Directed cell migration could be easily examined in these strips; half the coverslip was cleaned of the lipid before seeding the cells and several days later, after a confluent monolayer was formed on the glass, the strips were scratched in the film and the cells began to migrate in this narrow region.

It is not clear what characteristic of the surface of the lipid film is essential for its nonadhesiveness. Adhesion of cells to various substrates seems to be relatively independent of their hydrophobic or hydrophilic properties[7]. Electro-negativity of the surface of phospholipid film may play an important role[8]. Possibly the interaction of the cell surface with that of artificial phospholipid membrane may be considered as a simplified model of cell membrane to cell membrane interaction. In this connexion it would be useful to study cell interactions with films made of various types of lipids.

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Cycloheximide affects Memory within Minutes after the Onset of Training

WHEN mice are given brief discrimination training in a T-maze following intracerebral or subcutaneous administration of the protein synthesis inhibitors cycloheximide or acetoxycycloheximide, their learning curves are indistinguishable from saline-injected controls[1,2]. Retention measured 3 h after training is also identical in the drug-treated and control groups, but 6 h after training the drug-treated mice exhibit a striking impairment of retention[1,2]. These results suggested that cerebral protein synthesis is not required for retention for at least 3 h after training. We now report that using an alternative training procedure a cycloheximide-sensitive component of memory storage can be detected within minutes after the beginning of training. This suggests that in some circumstances cerebral protein synthesis may be required for normal expression of memory within minutes after learning has begun.

We trained mice in the Deutsch carousel[3], an automated discrimination training apparatus. Mice were secured by the tail
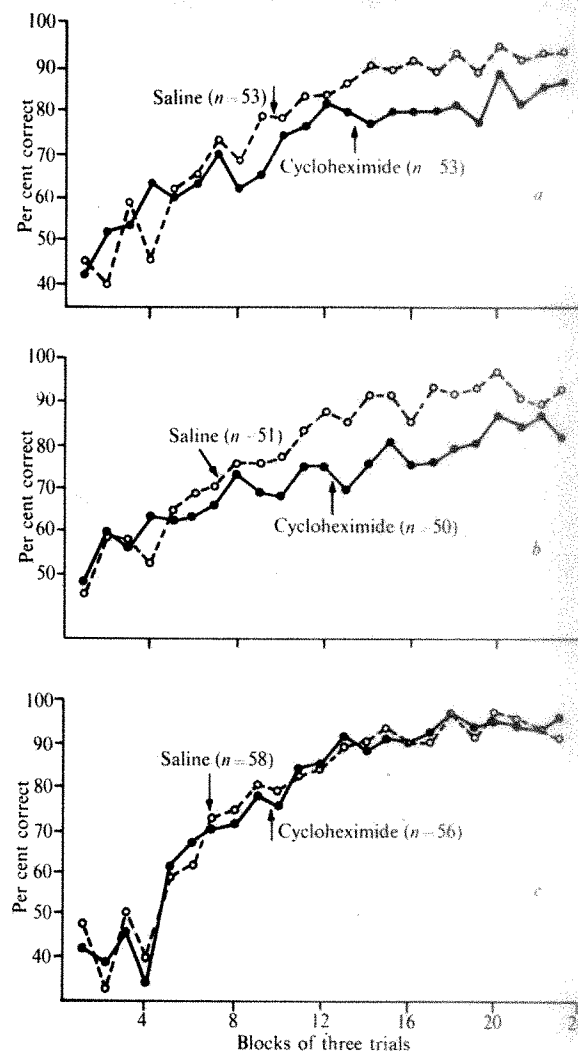
Fig. 1 Mice were trained for sixty-nine trials 10 min (a), 30 min (b) and 210 min (c) after subcutaneous injection of 120 mg/kg cycloheximide or saline. The resulting learning curves of cycloheximide-treated and saline-treated mice were divided into thirds (trials 1–23, 24–46, 47–69) and submitted to a two-way analysis of variance having repeated measures on one factor[10]. When cycloheximide was given 30 min or 10 min before training, both the effect of drug treatment (30 min $F=8.0$, 10 min $F=6.3$) and the effect of trials × drug (30 min $F=10.7$, 10 min $F=7.1$) were significant ($P<0.02$). When cycloheximide was given 210 min before training, neither the effect of drug ($F=0.1$) nor drug × trials ($F=0.4$) approached significance ($P<0.25$). Individual comparisons[10] indicated that during trials 1–23, the effect of cycloheximide on training did not approach significance in either of the conditions ($P>0.25$). Thus, the effect of cycloheximide given 10 min or 30 min before training is measurable only after twenty-three trials.

in the centre of a circular platform, facing the perimeter, and rotated for each trial to one of three positions. At each position, a mouse could escape shock by touching the smaller of two stainless steel objects. Details of this apparatus and training procedure have been described[3]. Mice hybridized from Balb/c females and C3H males were injected with 120 mg/kg cycloheximide or saline subcutaneously. Determination[4] of incorporation of ^{14}C-leucine into cerebral protein indicated that more than 95% of cerebral protein synthesis was inhibited 10–40 min after injection. When mice were trained for sixty-nine trials beginning 30 min after injection with cycloheximide or saline, their learning curves were not distinguishable for the first fifteen to twenty-five trials (Fig. 1). This observation corroborates our earlier reports that performance during initial training for up to twenty-seven trials in this task is not affected by cycloheximide[3] and that initial training in maze tasks, which requires fewer than twenty trials, is also not affected by this drug[1,2]. However, beyond the first fifteen to twenty-five
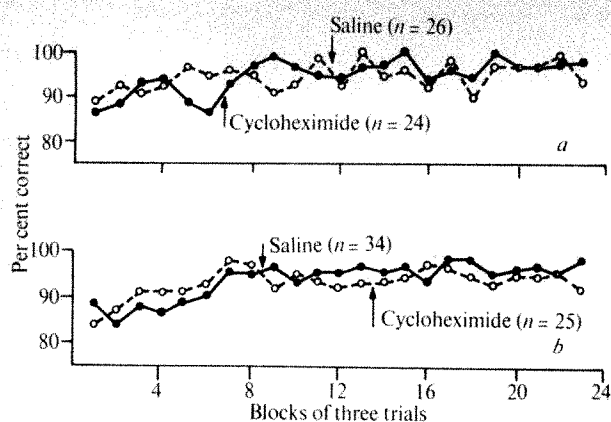
Fig. 2 Mice were trained for sixty-nine trials in the Deutsch carousel and then given a further sixty-nine trials 24 h later. Thirty minutes before retesting (*a*) or 210 min before retesting (*b*), mice were given 120 mg/kg cycloheximide or saline subcutaneously. A two-way analysis of variance with repeated measures[10] indicated that neither the drug effects ($F=0.01, 0.3$) nor the drug × trials effects ($F=2.3, 1.9$) were significant in condition *a* or *b* ($P>0.1$) for all comparisons. Thus, cycloheximide exerted no effect during prolonged testing of mice which had already been trained.

trials the learning curves diverge, and thereafter the cycloheximide group did not improve as rapidly as the saline group (Fig. 1).

The divergence of the learning curves at trials fifteen to twenty-five occurred about 40 min after drug injection. At about 45 min after drug injection, mice also become markedly hypoactive and remain so for several hours[5,6]. Because of the temporal coincidence of these effects of cycloheximide on training and on locomotor activity, we specifically investigated the possibility that retarded acquisition in cycloheximide-treated mice might be related to depressed motor activity. Mice were trained 10 min, rather than 30 min, after subcutaneous injection of cycloheximide or saline. Since training for sixty-nine trials takes approximately 25 min, hypoactivity does not develop in this condition until after training is completed. Thus, if locomotor depression is the cause of the acquisition deficit, the deficit should not appear. Alternatively, if the learning deficit in cycloheximide-treated mice is related to inhibition of cerebral protein synthesis, which is greater than 95% both at 10 min and 30 min after injection, the deficit in acquisition should be about the same in both conditions. Fig. 1 indicates that a deficit did appear when training began 10 min after injection and that the divergence in learning curves was first noticeable beyond trials fifteen to twenty-five, whether training began 10 or 30 min after injection.

We also trained mice 210 min after injection of cycloheximide or saline. Mice are hypoactive at this time[5,6] and are visibly sick, although only 80% of cerebral protein synthesis is inhibited at this time in this strain of mice. If the deficit in acquisition is due to locomotor depression or to cerebral abnormalities resulting from a period of extensive inhibition of protein synthesis, an impairment in acquisition should also be demonstrable in mice trained at this time. Alternatively, if the deficit which we have observed is due specifically to more than 80% inhibition of cerebral protein synthesis during training, a deficit might not appear in mice trained 210 min after injection. No deficit was observed in this condition (Fig. 1).

We also considered the possibility that cycloheximide might interfere with performance by simply preventing mice from ever executing a high percentage of correct choices in this task. Saline-treated mice which had been trained for sixty-nine trials were divided into matched groups and 1 day later were retested by exposing them to sixty-nine additional trials 30 min or 210 min after cycloheximide or saline. If protein synthesis inhibition or side effects of the drug make it difficult to achieve high levels of performance in this discrimination task, then

performance should be impaired by cycloheximide injection before retest. Alternatively, if the deficit is related to inhibition of protein synthesis required specifically for the development of memory during initial learning, then performance of an already established habit should not be impaired by cycloheximide injection before retest. The results indicate that cycloheximide had no measurable effect on performance of the previously learned habit (Fig. 2). All groups maintained performance between 85–100% for the entire session.

These results indicate that within minutes after the beginning of training improvement in performance may be antagonized by cycloheximide. The results further indicate that hypoactivity produced by cycloheximide is not the cause of this effect and that cycloheximide does not prevent a high level of performance if prior training has occurred. We therefore suggest that a memory storage process dependent on protein synthesis may be required for as long as improvement in performance within minutes after the onset of training. In other experimental situations[1,2,7-9], this may have been overlooked, because only brief training was given. Reasons why normal retention is observed for 3 h after training[1,2] in these situations have been considered previously[3].

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Dactylaria gallopava, a Cause of Avian Encephalitis, in Hot Spring Effluents, Thermal Soils and Self-heated Coal Waste Piles

THE hyphomycetous fungus *Dactylaria* (= *Diplorhinotrichum* = *Scolecobasidium*) *gallopava* (W. B. Cooke) Bhatt and Kendrick[1] was originally described as a causal agent of encephalitis in turkey poults[2]. Because of new outbreaks of encephalitis of turkeys and chickens caused by *D. gallopava* (H. G. Blalock, W. T. Derieux, L. K. Georg and M. Ranck, personal communications), the widespread occurrence of *D. gallopava* in natural and man-made heated habitats should be noted.

We have isolated *D. gallopava* from geothermal habitats and from self-heated coal waste piles (Table 1). The 393 samples examined represented a wide range of *p*H values (<2 to >10). The fungus was isolated from thirty-one samples, all acidic (*p*H 2.1 to 5.9), suggesting that this is its preferential habitat in nature.

Samples were enriched at 37 and 47–50° C using several natural and artificial substrates. Sabouraud dextrose agar (Difco) plates (pH 5.6), with 100 μg ml.$^{-1}$ of the thermostable antibiotic gentamicin sulphate, were best suited for detection and enumeration of *D. gallopava*; a distinctive reddish-purple pigment appeared in the agar beneath even young colonies.

Evidence for growth in natural habitats was obtained by observation of microscope slides which had been placed in hot spring effluents and thermal soils for differing periods of time, the habitats having a wide range of temperature (ambient to 87° C) and pH (1.7 to 8.4). At several hot, acid sites, a microbial mat composed of *Cyanidium caldarium* (a unicellular eukaryotic alga), *Dactylaria gallopava* and *Bacillus coagulans* formed on immersion slides; the structure of this mat was the same as on natural substrates. Structural and ecological relationships of the components of the mat will be reported elsewhere[3]. In aquatic habitats, impaction of the distinctive 1-septate, apiculate conidia of *D. gallopava* on the slides was followed by germination and development of radial microcolonies which could be traced to germinated conidia; a branched, septate mycelium subsequently developed. In soils, immersion slides bore conidiating colonies.

Further evidence for growth of *D. gallopava* in natural habitats is the occurrence in foam of its spores, germinated spores, hyphal networks traceable to spores and spores attached to conidiophores. This foam, which forms in turbulent regions on hot spring effluents, had the same pH value as the underlying waters and was only slightly cooler. One foam sample contained approximately 2×10^6 conidia ml.$^{-1}$ of the liquid obtained from the foam. Germinated conidia also occurred in microbial mats in hot spring effluents.

Occurrence of *D. gallopava* in coal waste piles in England has been reported[4,5]. We isolated the fungus from two of 250 samples from thirty-five self-heating coal waste piles in Pennsylvania and Indiana. Most of our samples were acid and were from sites having temperatures compatible with growth of *D. gallopava*.

Growth in pure culture occurred at both 20 and 50° C, although growth was slight at 50° C; rapid growth and conidiation occurred on Sabouraud dextrose agar at 37° C. To determine whether the apparent preference of the fungus for acid habitats was due to restrictive growth capacities at non-acid pH values, growth was measured in a malt extract medium adjusted to various pH values. Dry weight increase at pH 8.75 was excellent and was approximately the same as at pH 1.9 and at intermediate values; the fungus is therefore not obligately acidophilic. The fungus did not degrade filter paper at pH 3 or 7, nor did it clear Walseth acid-swollen cellulose[6] at pH 6.

H. G. Blalock and W. T. Derieux have established pathogenicity of our isolate 141-2 from Yellowstone National Park

(personal communication). Day-old turkey poults were inoculated intratracheally and the fungus was re-isolated from the brains of birds that died.

We conclude that *D. gallopava* occurs and grows in effluents of acid hot springs and in acid thermal soils; it also occurs in self-heated coal waste piles. Many species of thermophilic and thermotolerant fungi isolated from natural thermal habitats[7,8] similarly occur in man-made heated habitats far from natural thermal sites[4,9–11]. As temperatures in the range of mammalian and avian body temperatures exist in many geothermal sites, these habitats might be natural reservoirs for pathogenic microorganisms, and further search for pathogens in such locations is warranted.

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Table 1 Sample Sites which yielded *Dactylaria gallopava**

Sample site	Temperature†	pH‡
Thermal soil, Roaring Mountain, YNP§	42–43° C	4.5
Thermal soil, Solfatara Plateau, YNP	38.5–49.5	4.0
Thermal soil, Rush Lake Meadow, YNP	57.8–61.5	4.3
Thermal soil, Sylvan Springs, YNP	29	2.1
Hot spring effluent, Nymph Creek, YNP	50	2.8
Hot spring effluent, Sylvan Springs, YNP	48	2.9
Hot spring effluent, Ebro Springs, YNP	43	2.9
Hot spring effluent, Cyanidium Creek, YNP	46	3.0
Coal waste pile, Sonman, Pennsylvania	36–68	5.9
Coal waste pile, Mather, Pennsylvania	35–71	3.5

* Several sites yielded more than one positive sample.
† Using an electronic thermometer (Yellow Springs Instrument Co., Model 42 SC, with Model 408 "banjo" probe).
‡ By pH meters. Soil and coal waste samples were mixed with an equal volume of distilled water.
§ Yellowstone National Park. Rush Lake Meadow, Solfatara Plateau, Nymph Creek and Cyanidium Creek are unofficial names; exact locations and additional habitat data are available[12–14].

Thermal Regulation in Sail Lizards

THE extinct Order Pelycosauria contained several genera of reptiles characterized by extreme elongation of the neural spines of the vertebrae, which in life supported an area of membrane forming a "sail"[1–3]. *Dimetrodon grandis* was the end form of an evolutionary series of pelycosaurs that had tended to develop increasingly large sails[2]. Many suggestions have been made about the function of the sail, as camouflage among reeds while it waited for prey, for sexual display, or literally as a sail while swimming[2]. Romer and Price[2] first suggested that it served a mechanical function and strengthened the backbone, but Romer[3] later realized that the sail had evolved with features strongly suggesting an early attempt at temperature regulation. The spines are grooved anteriorly and posteriorly to house blood vessels carrying a rich supply of blood to the sail[3–5].

Dimetrodon grandis is found in the Autunian formation of the Permian of Texas. The environment was semi-arid with a xerophytic flora; yet enough water was present in certain areas to support a varied population of amphibians[2]. *Dimetrodon*

was the dominant carnivore, and possible prey included the herbivorous pelycosaurs *Edaphosaurus* and *Cotylorhyncus* and the amphibian *Eryops*[2]. Presumably, the environment was warm and sunny enough for the pelycosaurs to bask in the Sun in the normal reptilian manner[6], and it is possible that, as in arid areas today, there was considerable diurnal variation in temperature[7].

Assuming the present solar constant of 20,000 calories min^{-1} m^{-2}, the maximum rate of heating *Dimetrodon* would be 20 A/W K min^{-1}, where A is the projected area (m^2) and W is the weight (kg). Allowing for incomplete absorption, atmospheric attenuation and possible brightening of the Sun in the last 260 million years, a rate of heating of 10 A/W K min^{-1} was unlikely to have been exceeded under natural conditions. This is approximately the rate of heating in American alligators when exposed to the Sun[8]. The weight of *Dimetrodon grandis* was estimated by Romer and Price[2] as 250 kg. We have found that the lateral projected area is 1.88 m^2, the sail accounting for 1.15 m^2 of this. Taking 26° C as the voluntary minimum temperature and 32° C as the activity temperature[8], and assuming that *Dimetrodon* basked laterally to the Sun's rays in a similar manner to other reptiles[6,9], the value of the sail as a device to hasten heating can be quantified by using the formula above. The body temperature would have been raised from 26° C to 32° C in 205 min without the sail, but would have taken only 80 min with it.
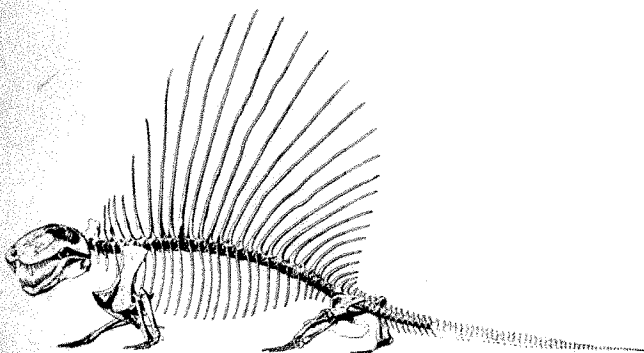
Fig. 1 Skeletal restoration of *Dimetrodon grandis* (from ref. 2).
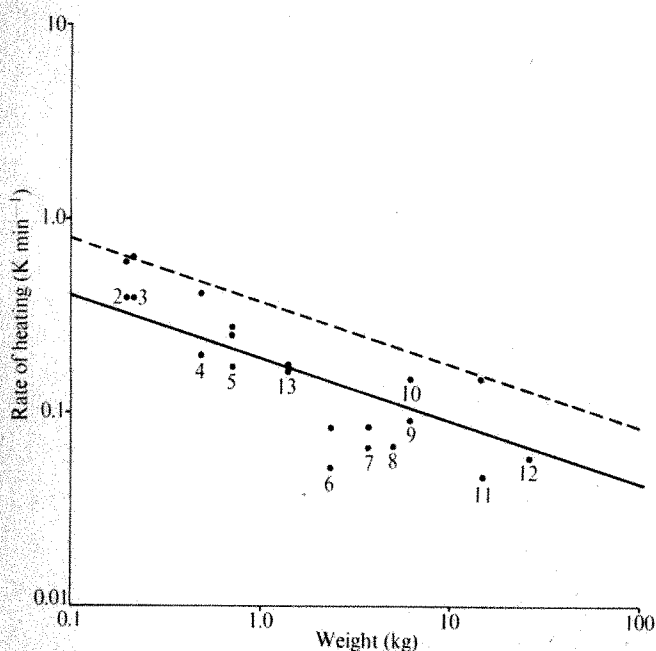
Fig. 2 Rate of heating of American alligators of different weights exposed to sunlight. Data from Colbert *et al.*[8]. Slope (———) is −1/3 (about 10 A/W).
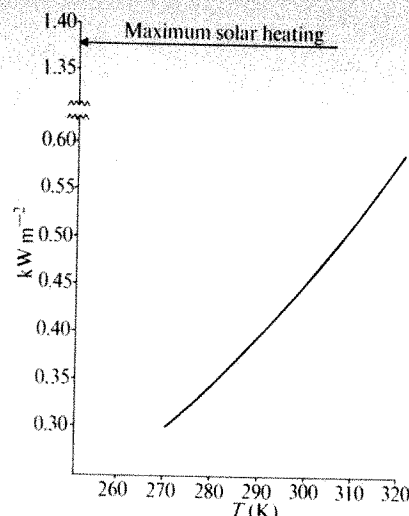
Fig. 3 Heat radiation from the sail of *Dimetrodon*.

The sail was also capable of radiating heat from the animal. To do this *Dimetrodon* would have assumed a position in which it presented a minimum area to the Sun, that is facing anteriorly towards it, allowing the sail to radiate to the sky from both its surfaces. The projected area exposed to insolation in this position is only 0.21 m^2. Living reptiles orientate in this manner[9] when their temperature rises above the normal activity range and approaches the critical maximum of 38° C to 43° C, according to the species.

The maximum radiation possible is shown in Fig. 3; at a realistic body temperature of 40° C it is 0.54 kW m^{-2}. Allowing for imperfect emissivity and radiation back from the environment, the net value is unlikely to have exceeded half this, but even so this still amounts to 0.6 kW being lost from the 2.3 m^2 area of the sail.

These figures lend quantitative support to the hypothesis[3] that the sail conferred advantage through thermal regulation. Faster attainment of the activity temperature in the morning was an obvious advantage to a carnivorous reptile feeding on other large poikilothermic animals. *Dimetrodon grandis* would have been able to reach an active state and attack prey while they were still torpid or sluggish. During the hot part of the day the sail would have acted to radiate away excess heat; this effect could be an important adaptation in a reptile which was too large to seek shade behind small stones or in rock crevices[9] in the manner of small living reptiles. In the evening *Dimetrodon* could have gained extra activity time, in comparison with a sail-less pelycosaur of the same A/W ratio, by restricting blood flow to the sail. The sail could therefore prolong the total time in which *Dimetrodon* could be active in any 24 h.

Our conclusions are reinforced if, as seems probable, the controlling adaptations had become highly refined. In addition to adjustments of blood supply, the degree of blackening may have been under nervous or hormonal control. Some lizards[9] which are black when basking to catch the maximum radiant energy can change to white when oriented head-on to the Sun and emitting heat. It is possible that *Dimetrodon* (or indeed living reptiles) may be black in the infrared to radiate heat more effectively, while appearing white in visible light. Visible and infrared emissivities of *Dimetrodon* may have been separately adjustable according to the thermal state of the animals.

We thank Professor Romer for permission to use Fig. 1

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External Ocelli in Lepidoptera Previously Considered to be Anocellate

DORSAL ocelli are simple photoreceptors found in nymphal and adult hemimetabolous insects and adult holometabolous insects[1,2]. They were thought to have a variable distribution, and to be absent in many representatives of several insect orders ; in Lepidoptera several families have been considered to be entirely or partially anocellate[2-4]. In sphingids it has been reported that their large superposition eyes have assumed the function of the ocelli[4], but it is now known that the sphingids are not anocellate. Ocelli were described within the dorsal protocerebrum in the adult of *Sphinx convoluvi* by Berlese[5] and recently internal ocelli have been reported in several adult sphingids, saturniids and citheroniids[6]. There have been no descriptions of external ocelli in sphingids, saturniids, citheroniids, or any Ropalocera[7].

We re-examined the structure of ocelli in moths previously described as being anocellate. Removal of scales on the vertex of the head posterior to the antennae and dorso-medial to the compound eyes revealed a small pair of external corneal lenses (Fig. 1a and b). These convex structures were located at the bottom of a round cuticular depression about 26 μm diameter. Similar, slightly smaller structures were found in the several species of butterflies examined (Table 1).

Longitudinal sections through this external cornea revealed several underlying cells believed to be retinular cells (Fig. 1c). In the sphingid specimens observed, a nerve branch arising from the bulb of the internal ocellus could be traced to the external structure (Fig. 2). Although similar nerves were not observed in all specimens examined, the possibility of their existence cannot be ruled out at this time. Similarly, internal ocelli have not been detected in all Ropalocera; they are, however, present in Hesperiidae and a structure believed to be an internal ocellus has been observed lying on the dorsal side of the protocerebrum in the pierid, *Colias philodice* (Fig. 3). We believe similar structures will be found in other butterflies as well.

This is the first report of external ocelli in Lepidoptera previously described as being anocellate. Eaton[6] reported that removal of the scales on the vertex of certain sphingids,

Fig. 1 *a*, Scanning electron micrograph of *Manduca sexta* (Lepidoptera: Sphingidae) head showing the two corneal lenses. The posterior of the head capsule is up. Bar equals 100μ. *b*, Higher magnification of the cornea on the left side of *a*. *c*, Light micrograph of a longitudinal section through the external ocellus of *Calasymbolous excaecata* (Lepidoptera: Sphingidae) showing cornea and a nerve extending from the cells beneath the cornea. Bar in *b* and *c* equals 20 μm. c, Cornea; cl, probable retinula cells beneath cornea; cu, cuticle; nc, nerve leading to cells beneath cornea.
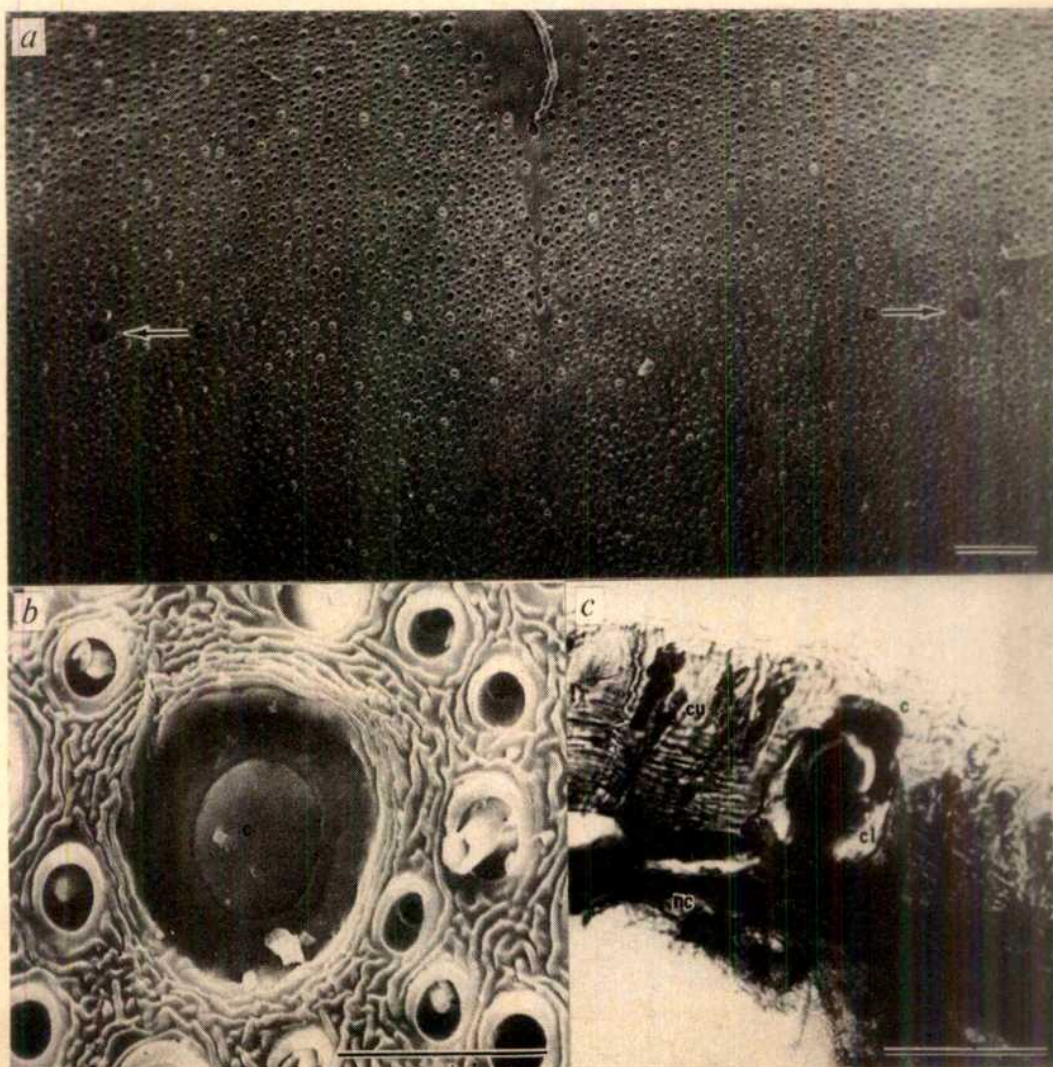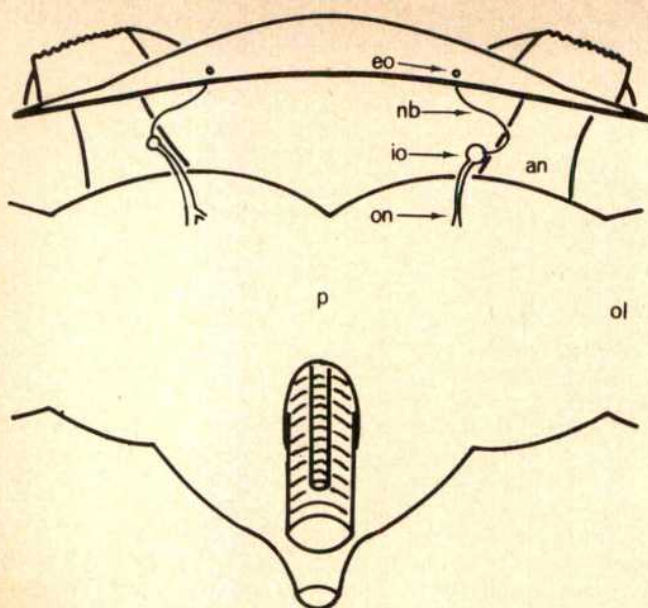
Fig. 2 Posterior view of the brain of *M. sexta* showing the internal ocellus and the nerve branch to the external ocellus. The asymmetry between the two ocelli is an example of the variation in structure frequently observed. an, Antennal nerve; eo, external ocellus; io, internal ocellus; nb, nerve branch; on, ocellar nerve; ol, optic lobe; p, protocerebrum.

saturniids and citheroniids revealed an evenly pigmented cuticle with no lens-like structures present. This earlier oversight was due to the small size and the coloration of the corneal lenses along with the fact that they are not located in the usual position of the lepidopteran ocellar cornea. In our study all "anocellate" Lepidoptera examined possessed small external ocelli.

The presence of a nerve branch from the internal to the external ocellus in some moths indicates either ; the presence of synapses of sense cells of the external ocellus with second order neurones whose somata lie in the brain, or extension of sense cell fibres whose somata lie in the internal ocellus (which is unlikely) or the presence of internuncial neurones between sense cell fibres from the external ocellus and fibres from somata within the brain (which is improbable). We considered the possibility that the nerve branch might act as a light-guide to conduct light to the internal ocellus but we rejected it owing to the tortuous route taken by this nerve.
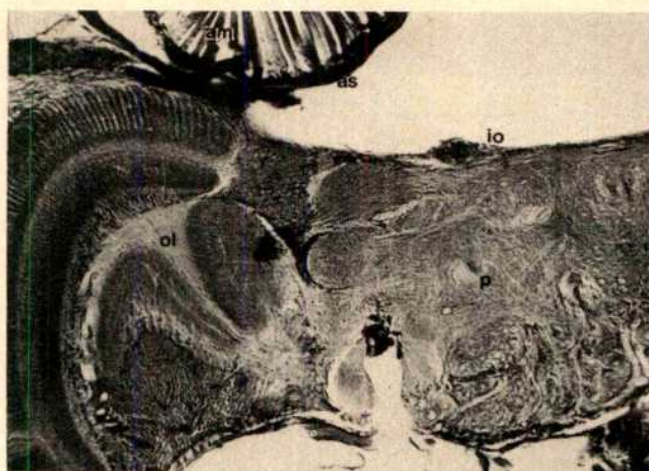
Fig. 3 Light micrograph of a frontal section through the head of a clouded sulphur butterfly *Colias philodice* (Lepidoptera: Pieridae) showing the left side of the protocerebrum, optic lobe and possible internal ocellus. am, Antennal muscles; as, antennal sclerite; io, internal ocellus; ol, optic lobe; p, protocerebrum.

Table 1 Lepidoptera reported to be Anocellate having External Ocelli

Heterocera

Sphingidae:
  Calasymbolous amyntor
  C. excaecata
  C. myops
  Darapsa myron
  D. pholus
  D. versicolor
  Herse cingulata
  Hyloicus chersis
  H. drupiferanum
  Lapara coniferarum
  Manduca quinquemaculata
  M. rustica
  M. sexta
  Pholus achemon
  P. pandorus
  Spectrum lineata
  Sphinx jamaiciensis

Saturniidae:
  Actias luna
  Automeris io
  Telea polyphemus

Citheroniidae:
  Anisota rubicunda
  Citheronia regalis
  C. sepulchralis
  Eacles imperialis

Arctiidae:
  Lithosiinae
    Hypoprepia miniata

Ropalocera

Papilionidae:
  Papilio polyxenes
  P. troilus

Pieridae:
  Colias eurytheme
  C. interior
  C. philodice
  Pieris rapae

Danaidae:
  Danaus plexippus

Satyridae:
  Cercyonis pegala

Nymphalidae:
  Euphydryas phaeton
  Limenitis archippus
  Polygonia comma
  Speyeria aphrodite
  S. cybele
  S. diana
  S. idalia
  Vanessa atlanta

Libytheidae:
  Libytheana bachmanii

Lycaenidae:
  Celastrina argiolus pseudargiolus

Hesperiidae:
  Epargyrens clarus
  Thorybes pylades

Perhaps the most significant aspect of our study is the presence of an external ocellus in "anocellate" Lepidoptera which in certain moths is also connected to the internal ocellus by a nerve branch. The possibility of a two-part ocellus in these moths therefore exists.

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BOOK REVIEWS

Mathematical Metaphor in Development

Stabilité Structurelle et Morphogénèse: Essai d'une Théorie Générale des Modèles. By René Thom. Edited by A. S. Wightman. Preface by C. H. Waddington. Pp. 362. (W. A. Benjamin: New York; Addison-Wesley: Massachusetts, November 1972.) $28.

THIS book by one of the world's foremost geometers is remarkable in many ways, but perhaps most notably for the breadth of the enquiry undertaken and for the unity and coherence of vision which are achieved. What we are offered is a new mathematical metaphor, created by Thom in response to the challenge of rendering intelligible the world of structure and form. The primary inspiration for this came from reading the works of biologists such as D'Arcy Thompson and C. H. Waddington on the origin and nature of organic form as revealed in plant and animal morphogenesis. The strong geometrical imagery of these writings provided the germ for a mathematical theorem which is the foundation of a complex edifice of analytical constructs applied sometimes with insight, sometimes without, to a wide range of biological problems.

Despite certain shortcomings, the book gave me a sense of liberation and enlightenment akin to what I imagine Ptolemaic astronomers may have felt when offered Copernican heliocentric geometry as an alternative to the endless epicyclic calculations required by the geocentric picture. The Ptolemaic system that I feel burdened by is biological model-building which proceeds from the kinetics of molecular and cellular interactions through non-linear differential equations to the study of their solutions in the neighbourhood of singularities. Created by Newton and Leibnitz in response to the necessity for a quantitative rendering of the Copernican model, the differential calculus was not intended to deal with discontinuity and structure but with continuous, smooth planetary motions. Poincaré initiated a more general approach to the study of discontinuities or bifurcations of dynamical sys-

tems about 100 years ago, and it is the recent flowering of this method in the hands of Russian, French, and American mathematicians which provides the context for Thom's work. This shifts the focus from continuity to discontinuity, facing directly the problem of describing mathematically how singularities arise in natural processes and generate discrete shapes and forms (including symbols). Since these processes vary with the initial state, it is necessary to forge an analytical tool which allows one to explore the possible structures which can arise in a given dynamical context and the stability of their structural emergences or unfoldings (hence a systematics for their classification). This is what Thom achieves in his basic theorem, presented in some detail in chapter 3. I cannot pretend to have followed all the details of this theorem, but, as it is the basis of the whole book, a few words of description are appropriate.

It is acknowledged by the topological *cognoscenti* that very little is known about the general properties of dynamical systems as described by the flows or trajectories on a manifold. Faced with an amorphous state of general theory, a mathematician must be guided by his insight and intuition in seeking constraints which generate new mathematical structures in terms of which the "real" world can be represented. Thom uses two fundamental postulates: (1) a general one of structural stability which embodies a basic principle about legitimate, intelligible models of natural process (hence the sub-title of the book); and (2) a specific hypothesis which requires that the dynamical systems studied be describable by gradient fields of potential functions. The mathematical entities which emerge from these constraints are the seven (and only seven) elementary ways in which the particular class of dynamical process considered by the theorem can give rise to discontinuities or singularities (called catastrophes) in ordinary space-time, generating recognizable structures or forms in a stable

and repeatable manner. These discontinuities act as local organizing centres of the dynamical process, a space-time structure emerging in a defined manner as described by the universal unfolding of the singularity (or its enfolding, if the process is reversed). If the dynamical space is insufficiently polarized for there to be a local coordinate system, then another much more complex set of singularities can occur, called generalized catastrophes. Their properties have not yet been analysed in any detail.

The postulates of the theorem have been criticized on the grounds that they are both too general (for example, they are relative to an unspecified diffeomorphism on the space one uses to describe a process of interest, such as a biochemical concentration space), and too specific (for example, gradient field systems are a very restricted set of those that are possible). I think these criticisms tend to cancel one another out. The main point is that these postulates result in a geometrical model which is radically (that is, at the root) non-linear and lends itself naturally to description in the same language as that used in morphogenesis: organizing centres, polarity, morphogenetic fields, the development or unfolding of a centre, interactions between competing organizers or attractors and so on. Thom's own position is essentially Aristotelian (he would prefer Heracleitian or Cartesian): the primary qualities demanded of a model or a metaphor besides precision and rigour are intelligibility and appropriateness for the description of natural, and particularly biological, process. Quantitative power, computability, is secondary to understanding and meaning. Every concept Thom uses to supplement the basic theory of catastrophes in order to give it the dynamic plasticity and complexity required for biological explanation, such as the concepts of thermodynamic coupling, resonance, phase transition, and so on, is used in a purely descriptive spirit and will no doubt irritate those looking for an exact quantitative

test of the model. Such a test is not available for the principal reason that as yet no calculus exists which allows one to use Thom's theory of the unfoldings or enfoldings of organizing centres of catastrophes in a computational rather than a geometrical manner. Thus any test of the theory at this stage in its development must be qualitative, in terms of intelligibility and appropriateness, and this is difficult for minds more receptive to local goodness of fit than to global meaning. But let me try.

I think it would be fair to say that practically every specific biological process which is described and analysed by the theory advanced in this book is more thoroughly and adequately accounted for at the moment by a model constructed in terms of the concepts germane to the level of the problem, whether molecular, cellular, physiological, genetic, or psychological. There are many points where I find the application of the theory excessively literal, rather like regarding the burning of a candle and the respiration of glucose as identical; which is not to deny a fundamental similarity. For example, in the treatment of the nucleus as a chemostat (page 279) the interaction of chromosome and cytoplasm is interpreted as a hydrodynamic singularity, a diffusional shock wave across the membrane which persists until nucleo-cytoplasmic control equilibrium is attained. I find it difficult to imagine such a shock wave lasting for periods of hours, the relaxation time of such responses, given the rapidity of diffusional equilibration. Again, the attempt to provide a Lamarckian interpretation for the evolutionary origins of organs, proteins, and genes and the appeal to plasmagenes is basically unconvincing. There are undoubtedly ways in which heritable metastable states of chromosomes, membranes and organelles can be induced by physiological stress ("shock waves"), but these must be thought out much more subtly in relation to current knowledge than we are given here. Chapters 9–12 in fact are written in the style of an extended, free metaphor and a great deal of their content cannot, I find, be taken literally. On the other hand they are full of improvisation and rich in suggestion. For example, the analysis of the relationships between gastrulation in amphibians, reptiles, and birds (pages 180–184) is very ingenious despite inaccuracies of fact here and elsewhere (closure of the blastopore in amphibia takes hours, not seconds; mesoderm induces ectoderm not *vice versa*), and suggests some interesting comparative embryological experiments, at least between the cold-blooded genera.

This leads us to ask the question whether Thom's theory tells us anything we did not already know in more detail. I think it does, in two important respects. First, although it does not explain the intricate architecture that evolution has built into biological structure-generating processes, the mathematical theory is capable of such elaboration in relation to the details of the universal unfolding of a singularity or organizing centre. In this sense it suggests a direction for the development of a calculus that copes easily with non-linearity and discontinuity, with stability and structure. And second, the theory directs our attention to the very difficult problem of origins: what is the natural basis for the emergence of the extraordinary complexity of biological process? Thom believes with Heracleitus that nature is one: that the structures we see in the physical world such as the breaking wave or the whirlpool are generated by dynamical germs or centres that are geometrically similar to those operating in organogenesis or enzyme action, for example. The difference is in the detail of the unfolding of the singularity, the biological system exercising precise control via proteins, membranes, electrical or material gradients, and so on. This vision of continuity is most powerful in the relation which Thom describes between morphogenetic and behavioural fields in chapter 13, providing what I found to be an inspired though exceedingly sketchy conceptual framework for understanding how mind and symbol emerge from the biological substratum, the essential problem of structuralism. I suspect that it may be here that the theory could come most importantly to our aid, providing a bridge of intelligibility across a gap which at present seems so wide.

This book is to be regarded as outlining a method of inquiry, as Thom himself has emphasized; and this method may or may not succeed. In biology we will discover this only by working with the model, developing the requisite calculus and attempting to fit it to the biological data. An impressive example of this procedure is provided by E. C. Zeeman, a lucid exponent of Thomism, in his article in the book *Towards a Theoretical Biology* (edit. by C. H. Waddington), 4, 8; Edinburgh University Press, 1972). In the same volume there is an article by Thom on "Structuralism and Biology" (pages 68–82), while his article in volume 3 of this series (pages 89–116) gives the essence of the method in English. Even if this model fails, the sustained inspiration and the vast scope of the book put it firmly into the best tradition of natural philosophy, the search for a rigorous and meaningful synthesis of the fragmented strands of contemporary knowledge. B. C. GOODWIN

Infrared in Space

Infrared Detection Techniques for Space Research. Edited by V. Manno and J. Ring. (Proceedings of the 5th ESLAB/ESRIN Symposium, held in Noordwijk, The Netherlands, June 1971.) Pp. xi+344. (D. Reidel: Dordrecht, 1972.) Dfl. 90.

THE bulk of this book contains information and data on a variety of techniques and facilities used in balloon, aircraft, rocket and satellite borne infrared observations, and is divided into six fairly well defined sections. Giving some perspective to the technicalities that follow, it begins with a short review of results obtained in infrared astronomy up to the middle of 1971. A section follows on the currently used telescopes and related systems for upper atmospheric and space vehicles. Two balloon borne systems in operational use, of 30 cm and 39 cm aperture with magnetometer and star tracking guidance respectively, and systems of 32 cm and 90 cm for aircraft use are described. There are contributions on interferometry and radiometry from rockets and satellites and observational data on the spectral sky radiance as a function of altitude are provided. Also included in the section is a description of a helium cooled interferometer to measure the far infrared cosmic background radiation from balloon altitudes.

The third section deals with detectors, starting with a statement of fundamentals and the present state of the art and continuing with description and comparative performances of some cooled colometers and a contribution on the Josephson effect.

Fundamentals of space borne cooling systems are next reviewed and likely lines of development are indicated. One of the outstanding needs before astronomy in the middle and far infrared becomes possible from Earth satellites is the development of suitable long-term cryogenic systems for liquid helium temperatures. Although it seems a pity that this work contains only one contribution on the subject, it may perhaps be optimistically assumed that adequate solutions are nearer than the published literature would suggest. For all other than satellite systems the major problems seem to have been overcome, as indicated by the operational success of a number of helium cooled detection systems. A wealth of information follows on the design and fabrication of filters for far infrared work. Much of this section is devoted to the use of metal mesh filters and performance data are given on a number of practical designs.

A fairly full section is given on the use and principles of interferometer techniques and the book closes

with a short section of discussions.

The book contains a large amount of relevant information on the subject matter for those active in the field. As well as this, the layout and presentation are such that there is much to interest the non-specialist.

D. K. AITKEN

Ganglion Growth Factors

Nerve Growth Factor and Its Antiserum. Edited by E. Zaimis and J. Knight. (Papers presented at a Symposium held at University College, London, April 1971.) Pp. xi+273. (Athlone: London, June 1972. Distributed by Tiptree Book Services Ltd.)

THIS volume consists of a collection of two dozen papers presented at a symposium held not quite two years ago at University College, London. Its content reflects the excitement, uncertainties, and controversies of a newly and rapidly developing field and points the direction of future research.

Nearly twenty years ago Dr Rita Levi-Montalcini and her associates discovered protein factors which stimulate growth of ganglionic neurones both *in vivo* and *in vitro*. The startling effects of antibodies to these proteins on the development of the sympathetic nervous system indicate their physiological importance. During the last ten years other investigators have been stimulated to examine the nature and origin of the protein factors and the biochemical and physiological consequences of administration of the antibodies to these factors.

In the introduction, the editors have succinctly outlined the purposes and objectives of the symposium. The first section is devoted to work which has been done to define the nature and actions of the nerve growth factor, while a second section considers antibodies to NGF, and a brief third section deals with the problems in the assay of NGF and its antibody.

The opening chapters present in adequate detail the methods for purification and characterization of NGF from snake venoms and mouse submaxillary glands. These factors appear clearly different from each other. The well known biological effects of NGF are reviewed by its discoverer and her collaborators along with a report of more recent observations on the subcellular distribution of NGF. The effects of NGF on growth of sympathetic tissues are well illustrated in the paper by Professor Zaimis, after which the biochemical and fine structural changes induced in sympathetic ganglia *in vivo* and *in vitro* are reviewed.

The second section of the volume is concerned with the effects of inhibition by antibodies to NGF of development of the sympathetic nervous system. The consequences of immunosympathectomy on the tissue content and metabolism of amines, and cardiovascular responses and behavioural patterns (by motor activity on exposure to cold) and use of immunosympathectomy as a pharmacological tool, are considered. In the last brief section on assay of NGF and its antibodies, some pitfalls in assays are pointed out and the potential for development of new sensitive radioimmunoassays for NGF is indicated.

The various papers are not of uniform detail or quality, but this may reflect the uneven advance of a new field. The editors have not imposed stylistic restrictions on the authors. One feels that a report of discussions of the papers might have enhanced the value of the volume since discrepancies and differences of opinion (for example, the similarities and dissimilarities of NGF from different sources), although recognized, pass without comment.

This is a cohesive, well balanced volume which may be considered a milestone marking a point in the development of a new and exciting field. There are wide implications to embryology and plasticity of the nervous system. It should be read by those interested in the problems related to the development of the nervous system as well as investigators concerned with mechanisms of the sympathetic nervous system.

I. J. KOPIN

Pollution by Combustion

Emissions from Continuous Combustion Systems. Edited by W. Cornelius and William G. Agnew. (Proceedings of a Symposium held at the General Motors Research Laboratories, Warren, Michigan, September 1971.) Pp. x+479. (Plenum: New York and London, 1972.) $29.

IT is none too common to be able to read the papers from a serious symposium within a couple of years and so the publishers of these are to be congratulated. The excellent presentation, diagrams, graphs and photographs do much to add to the general worth of this collection of opinions from acknowledged international pundits in the field of combustion. Would-be readers must realize, however, that these papers—and their related edited discussions—require considerable knowledge of thermodynamics, in certain cases fairly advanced mathematics, and some acquaintance with gas turbine and furnace technicalities. Although the ultimate purpose of the symposium was a general review of pollution from these sources and what can be done to reduce it, the speakers dealt with how to do it in the intimate terms of their trades.

General Motors Research Laboratories has held fifteen annual symposia to review the "state of the art" of the various sciences and techniques related to heat engines. The meetings last two days and about sixty delegates are invited after careful selection with a view to bringing together the élite of the academic, industrial and governmental brains concerned with the theme of the year. The choice of the environmental effect of emissions from the combustion of fossil fuels was becoming topical in 1971 and is of paramount importance today.

The symposium was given in four sessions: "Modelling continuous combustion", chaired by J. P. Longwell of Esso Research and Engineering Company; "Pollutant formation and destruction processes", chaired by G. C. Williams of MIT; "Effects of operating conditions and fuel factors", chaired by A. H. Lefebvre of the Cranfield Institute of Technology; and "Power-plant emissions", chaired by P. S. Myers, University of Wisconsin. It would be invidious to name only some of the authors of the twenty-one papers, but the outstandingly clear, concise and objective symposium summary by W. G. Agnew gives a very clear picture of what was said; he also made a profound comment on the general understanding of the subject as appreciated internationally by the participants.

The first session showed the way in which flow through combustors can be partially simulated observationally with kinetic models and by mathematical analysis. The general impression one gets is that there is still a long way to go before models can be really useful. The second session was largely reports of research in progress on relating physical and chemical parameters for the further elimination of unburnt hydrocarbon waste and ways of tackling NO (nitrous oxide) formations. At present water injection seems the best, but rather troublesome, method of suppressing these corrosive products by keeping the temperature below their formation level. However, from the third session, it appeared that such cooler gases can mean less than stoichiometric combustion— and, inevitably, unburnt hydrocarbon contaminants. The papers suggested, in fact, a temperature "slot" for combustion between 1,500–1,800 K in order to give the "purest" efflux. Control of visible smoke, the hydrocarbon and CO residue, is now being put into practice, beginning before ignition with vaporizing fuel injectors like those fitted in the latest Olympus in Concorde 02, which flew in January of this year.

In the fourth session, a paper on how

emissions from stationary boiler power-plants are being controlled was an interesting insight into other people's problems. The remaining papers in this section covered gas turbine, steam and Stirling-cycle powerplants for vehicles, with a fascinating one about the work of the General Electric Company (US) on the control and reduction of emissions from aero gas turbines. From this company's experience it would appear that the engine makers are on the last lap—reducing that reek of unburnt kerosene from idling engines which assails the passenger at every modern airport.

A very useful reference for any company technical library, or for a college —bearing in mind that much of the material will be out of date in five years —but a trifle expensive for the individual's purse. JAMES HAY STEVENS

Madness and the Community

A History of the Mental Health Services. By Kathleen Jones. Pp. xiii + 414. (Routledge and Kegan Paul: London and Boston, December 1972.) £5.

"HISTORY," said Henry Ford, "is bunk." In spite of Professor Kathleen Jones's modest supporting conclusion that the only lesson to be learned from the past is the unpredictability of change, her splendid book drives the reader relentlessly to a number of invaluable general deductions. Perhaps the most important of these is that progress, seen in historical time, is advancing in spiral fashion, with the real forward movement along the axis being agonizingly slow compared with the apparent speed of advancement round the circle. A corollary of this is that the defects of one system of care are only too easily thought to be remediable by replacing it with a "new" system, which history reveals has already been tried and found to have its own defects.

This important book succinctly traces the evolution of attitudes to the mentally ill and the mentally handicapped through the documentary evidence available to the historian. What might otherwise be a dull catalogue of reformist speeches, parliamentary debating points, and successive legal enactments is brought to life by illuminating personal anecdotes. I am still haunted by the description of William Norris, who was confined continuously for nine years at Bethlem in a special iron apparatus which effectively prevented all but the smallest movements. On discovery in 1813, he was found to be quiet and rational, able to hold an intelligent conversation, and to read with comprehension. In

case the reader is inclined to dismiss such extremities of treatment as belonging to the past, I would remind him that even today nursing shortages often compel staff to put violent patients in solitary confinement in small cells, when technical treatments well known to be effective in modifying such disturbed behaviour could be used if sufficient skilled staff were available.

No literate person should neglect a close examination of Professor Jones's book, for its lessons are of general importance. Perhaps all schools should make it their major study of social history. Imaginatively treated, its subject matter could make a strong impact on a new generation who might then make the sustained effort necessary to resolve the underlying problem: constructing a society with a different value system, in which the understanding of people's needs makes neglect of any section unlikely. We must remember that the weak and the poor are under-privileged because we are over-privileged. We have devised a set of rules for an economic competition which ensures that we inevitably win and they inevitably lose.

Community care is the currently favoured panacea for the evils of asylums built by a previous generation to rescue pauper lunatics from community neglect. The cynic will conclude, after reading this history, that it is possible to neglect the mentally disordered in two ways: we can shut them up in remote, impoverished institutions, or we can push them out into the uncaring anonymity of the urban environment. Either way we can assume it is for their good, especially if the service doesn't cost the rest of us too much and we don't actually have to be involved. And when some enterprising journalist uncovers a few scandalous cases, we can always comfortably indulge in moral indignation, especially if someone else can be conveniently scapegoated.

Community care, then, history tells us, is not worse, nor necessarily better, than institutional care. Care is the operative word. At a time when pride is being taken at the fall in the number of psychiatric beds, the number of people in prison and the number of urban homeless are rising. We can only be certain that the quality of life of the mentally disordered is improving, and goes on improving, relative to the rest of us, if we base our monitoring system on a complete case register which enables us to follow people's progress and to supply their needs through a flexible system of treatment and care facilities of a high standard. The public must not be allowed the comfort of ignorance, nor short-lived concern after scandalous revelations. They must be constantly reminded of the needs of local people and the cost of

the provision of satisfactory services.

The problem can then be seen in its proper historical perspective—the mentally ill and the mentally handicapped are neglected by us. Unless we vote with our money, and personally befriend the disordered and the deviant, the next two hundred and fifty years will be much like the last.

The question this book poses is, do we care? JACK BAVIN

Distributions

Distributions in Statistics: Continuous Multivariate Distributions. By Norman L. Johnson and Samuel Kotz. Pp. 331. (John Wiley: New York and London, November 1972.) £7.50.

THIS is the fourth of a series in which the authors systematically review what is known about statistical distributions. The three earlier books dealt with discrete distributions and continuous univariate distributions (two volumes). This present volume, undoubtedly the toughest, completes the set; multivariate discontinuous distributions were covered in the first volume.

There is a sharp contrast between the wealth of mathematical forms with which we can express the frequency or probability distributions of univariate theory and the relatively few tractable forms available in multivariate theory. The number of parameters concerned increases alarmingly with the dimension of the distribution—even for the simplest case, the multivariate Gaussian (normal) form, the parameters increase as the square of the dimension number. The evaluation of numerical probabilities by integration is a formidable task even for two dimensions and even with the aid of the electronic computer. Some entirely new types of problem arise which are not encountered in univariate theory; for example, finding the distribution of the eigenvalues of a covariance matrix, which are not, unlike most statistics, algebraic functions of the observations. Altogether, the theory of multivariate distributions poses the most difficult problems in mathematical statistics.

One therefore gives an unqualified welcome to this book, which systematically reviews the present state of knowledge and pulls together a somewhat scattered literature in a consecutive development. As a textbook it would be heavy going except for the specialist. As a work of reference it is invaluable —over 700 titles are given. A comprehensive coverage of such a kind is to some extent a labour of love and statisticians everywhere should be grateful to the authors for the amount of effort which has gone to the completion of this work. M. G. KENDALL

Biological Compartments

Compartmental Analysis in Biology and Medicine: Kinetics of Distribution of Tracer-labelled Materials. By J. A. Jacquez. Pp. xiv+237. (Elsevier: Amsterdam, London and New York, 1972.) Dfl. 77.50; $24.25.

COMPARTMENTS in a system interact with one another and perhaps with the surrounding environment. A compartment is an amount of material acting kinetically like a distinct well-mixed amount of the material. Separation between compartments does occur in various biological systems, for chemical as well as physical reasons. Compartments can be such things as plasma, interstitial and intracellular spaces. Hence the mathematical study of compartmental system models is useful, that of linear systems having counterparts in other areas of applied mathematics.

Inevitably the practical interpretation of compartmental analysis raises difficulties and arguments, and systems of order higher than linear are not easy to analyse. Nevertheless this book is an interesting survey of the present state of the art.

Necessary basic mathematics, covered in early chapters, comprises linear differential equations, vectors and matrices, and Laplace transforms: considerable facility in applying all these is needed to understand the book. This will indicate the appropriate level of readership.

It is in chapter 5 that biological interest really becomes aroused, by a study of radioactive tracer movement in steady state systems under suitable (and not unreasonable) assumptions. Henceforward, numerous references are made to the massive list of 455 papers (including some books) which appears at the end of the volume. This list is an excellent feature, but its presence only serves to make one wonder why space could not be found for answers to, or brief discussion of, the exercises at the ends of chapters.

Chapter 6 is concerned with systems partly compartmental and partly flowing, for example in some respiratory studies. Analysis in terms of experimentally observable functions can only be approximate, but does take the form of a compartmental system. Chapter 7 considers how one might set up a compartmental model from experimental data—very salutary after the almost entirely mathematical nature of the early part of the book—and chapter 8 introduces biological problems of varying complexity, and their solution by these methods.

After these two more practically biased chapters, the author moves from linear systems to introduce cases where experiments are long-term and so must allow for such things as daily (24-h) periods in bodily functions. Unfor-

tunately too, biological systems have a habit of containing random components: thus drug therapy has randomness in times of application, and even in amounts. Finally, the author picks a few points out of control theory, and in an interesting chapter 14 discusses some examples of compartmental control systems. G. M. CLARKE

Microcapsules not Cells

Artificial Cells. By Thomas Ming Swi Chang. Pp. xiv+207. (Charles C. Thomas: Springfield, Illinois, June 1972.) $16.

THE eye-catching title of this book immediately evokes curiosity and is likely to lead one to suppose that what may be predicted as achievable well beyond AD 2000 has already been accomplished in some quiet corner unbeknown to everybody. This is to some extent promulgated by the editor's preface connecting the studies with the synthesis of cells. Reference is made to forms of life on other planets and that the basic unit of such life could be different from the cell we know. All this seems to herald the shape of things to come in the book.

Authors are aware that the inclusion of a fashionable word in the title of a paper will send up the requests for reprints. A fashionable word is "cell" and in biology it stands for an extraordinary piece of machinery organized at the molecular level at a complexity that is almost beyond our belief and understanding. In the author's preface of the book we read: "Back in 1956 I was surprised to find that despite the fundamental importance of cells serious attempts had not been made to use available knowledge to investigate the feasibility of preparing artificial cells". We read on to find that "equipped with a borrowed clinical centrifuge, a few chemicals, a few glasswares and a few frustrating months" the author came up with samples of artificial cells. Each consisted of haemoglobin and enzymes from red cells enveloped in an ultrathin spherical polymer membranous bag of cellular dimensions. This comes as something of an anticlimax to anyone who takes the title of the book too literally.

The honest and exceedingly interesting theme of the book is the potential use of packaged enzymes and detoxicants. The membrane is constructed to allow entry of substrate and the passage out of the product while retaining the enzyme. Toxins would pass through the membrane and become adsorbed onto contained charcoal. Emphasis is laid on the membrane being inert and how enzymes safely kept within this membrane would not be able to elicit an immune cellular response. The approach holds much promise in bio-

medical research and clinical therapy.

There is an enthusiasm pervading the book which makes one overlook a certain amount of repetition. The spectulations in chapter 1 would have been better left to the end. The next chapter deals with the procedures for encapsulating microdroplets of cell products, and chapter 3 with the biophysical properties of the different kinds of membranes that can be produced. The experiments described in chapters 4 to 9 are certainly interesting; for example, urease in dialysis bags injected intraperitoneally can act efficiently on endogenous urea, converting it into ammonia; mice with a congenital deficiency in catalase can be furnished with this enzyme; tumours dependent on asparagine could be denied this substance by the presence of asparaginase-loaded dialysis bags. Substitutes for red blood cells bring one up against the importance of not using artificial membranes to which platelets adhere. The use of microcapsules containing charcoal instead of the two-compartment system of the kidney machine to trap waste metabolites seems practical enough, but one is left with the underlying feeling that the safety of the conventional machine is more important that ridding the blood of waste at a faster rate with "artificial cells". But, even so, the general idea of "artificial cells" being used in medical therapy is intriguing and I should imagine that practitioners in this field will welcome this book which draws attention to the state of progress so far made towards what is a difficult target.

B. M. JONES

Whence the Moon

From Plasma to Planet. Edited by A. Elvius. (Proceedings of the Twenty-first Nobel Symposium held in Salysjobaden, Sweden, September 1971.) (John Wiley: New York and London; Almqvist and Wiksell: Stockholm, October 1972.) £10.45.

AT the end of the Apollo manned lunar exploration programme scientists realize that they are on the verge of further exciting discoveries about both the history of the Moon and the origin of the solar system. Many fast-acquired, hard facts about the Moon have been creamed off by investigators using Apollo and Luna data. More subtle facts remain to be prised from the returned samples; and increasingly reliable interpretations will surely derive from continuing studies of lunar rocks and photographs and from the fascinating records now being accumulated via the Apollo experimental stations which continue to function automatically on the Moon's surface.

Lunar elemental abundances point

strongly to the Moon's never having been one part of the Earth: they are indicative, rather, of a Moon which originated from a nebular condensate under rather particular conditions in space. Studies of the ways in which plasmas and gases and particulate clouds behave under the action of an early solar wind are therefore of extreme importance if we are to learn more about the origin of planets—including the Earth itself.

How do atoms and molecules react in interstellar space and in the upper atmosphere of the Earth? What is the respective importance of electric phenomena and gas-dynamical forces in the early solar system? What is the accretion mechanism and the irradiation history of meteoroids? How were asteroids and comets formed? These are some of the fundamental questions raised by the experts who contributed to this volume.

Much may be learned—and cheaply in comparison with the cost of the manned spaceflight programme—by careful, protracted analyses of the smaller objects in the solar system: the dust in the upper atmosphere and in space, the asteroids, and the satellites of other planets. This may be regarded as a realistic view of one of the next steps that scientists may take in their continuing attempts to discover the origin of the planets.

This excellent book, for solar system specialists, physicists, chemists and astronomers, details how these problems are being tackled. At the end of each technical paper, it records valuable discussions between participants at the Nobel Symposium 21. Names such as Alfvén, Anders, Arrhenius, Massey, Millman, Petrov and Runcorn feature in the main text and in the discussions; and the book is undoubtedly well worth the price.   G. FIELDER

Homage to Meyerhof

Molecular Bioenergetics and Macromolecular Biochemistry. Edited by H. H. Weber. Pp. viii+197. (Meyerhof Symposium, Heidelberg, July 1970.) (Springer: Berlin and New York, 1972.) 79 DM; $25.10.

"DISTINCTION develops if nurtured by distinction," wrote Sir Hans Krebs (*Nature*, **215**, 1441; 1967) in tracing the factors that contribute to the making of successful scientists. It is thus perhaps not surprising that, among those who were Otto Meyerhof's former pupils and associates, or whose work was in some way profoundly influenced by him, and who gathered in Heidelberg in July 1970 to commemorate the life and work of that great biochemist, were seven Nobel Laureates as well as many

others who have made major contributions to biochemical knowledge. And it is, perhaps, also not surprising that the lectures given in this symposium are uniformly good: after all, here are the masters, talking about their own achievements. Thus, after a biographical sketch of Meyerhof (by his first pupil, H. H. Weber) and of his ancestry (by H. A. Krebs), there are lucid surveys of the structure and mechanism of action of aldolase (by B. L. Horecker), of the multi-enzyme complexes involved in fatty acid synthesis (by F. Lynen), of chain initiation factors in protein synthesis (by S. Ochoa), and of the amino-acid polymerizations involved in the formation of gramicidin and tyrocidin (by F. Lipmann). There are two fine papers on the structure (by K. C. Holmes) and the activity (by Annemarie Weber) of the actomyosin system of muscle. A fascinating discussion of the genetic basis of carcinogenesis (by L. Sachs) is followed by three equally fine papers on chemical (by M. Eigen) and physiological (by W. Hasselbach and, *in absentia*, by D. Nachmansohn) aspects of membrane processes. As an act of scientific homage to, and of pious remembrance of, a great biochemist and an obviously much-loved person, this symposium cannot be faulted.

One also cannot but applaud the peculiar appropriateness of the occasion. In 1968, the Volkswagen Foundation endowed an Otto Meyerhof Chair at the Weizmann Institute of Science, in Rehovot (Israel), to honour the memory of Meyerhof and to strengthen the relations between Israeli and German scientists. The symposium was planned, at the suggestion of Professor D. Nachmansohn, to commemorate that event, with the participation of German and Israeli scientists: indeed, one of the lecturers, Professor Sachs, is the first holder of the Meyerhof Chair. The symposium was accordingly arranged by a group of the Weizmann Institute, in consultation with Nachmansohn, Ochoa and the Organizing Chairman; it was sponsored by the Institute and the German Gesellschaft für Biologische Chemie. Nothing, surely, could have been more fitting to the occasion and more appropriate to the intention.

But do the proceedings of this symposium make a satisfactory book? With genuine regret, I must conclude that they do not. Such coherence as there is is provided solely by the sentiments of the occasion: as apparent from the contents listed above, there is no cohesive scientific theme. And, alas, there is also little novelty. The substance of much of the material has appeared in print on previous occasions and is now re-reproduced. Indeed, the German text of one excellent lecture is illus-

trated by diagrams, captioned in English, that must surely be familiar to most likely readers of this book and that have obviously been taken directly from another and widely-read publication.

Although this volume will be rightly treasured by those who attended the symposium, as a record of a unique occasion, I cannot imagine that there will be many private purchasers of this very expensive little book.

H. L. KORNBERG

Distribution Theory

Multivariate Analysis. By Anant M. Kshirsagar. Pp. xiv+534 (Marcel Dekker: New York, July 1972.) $19.50.

THIS book covers the advanced theory of multivariate analysis, concentrating to a large extent on distributional problems. It is a somewhat frightening volume to glance through, as inevitably it has many pages of complicated algebraic expressions; I approached it with some trepidation. It must be confessed, however, that Professor Kshirsagar handles his material so clearly and logically that difficulties are eased. It would be misleading to suggest that they vanish; this is a hard book to read. It is aimed largely at the postgraduate student of mathematical statistics.

It is also misleading to suggest that practical workers seeking guidance in the use of multivariate analysis would find the book helpful. Although the author occasionally presents a brief (and sometimes illuminating) paragraph on practical implications, the text is almost entirely theoretical.

In his presentation, the author makes great use of elegant matrix transformations and random orthogonal transformations, and many of his derivations are relatively neat and concise. Regression analysis plays a key role in the development, and Professor Kshirsagar emphasizes the central part canonical variables and correlations have in multivariate analysis.

Although practical illustrations are not given, there are plenty of references to papers where multivariate analysis has been used. Another feature is a large collection of theoretical exercises which will be valuable to the teacher and student. The appearance of the book is a little off-putting, it apparently having been reproduced directly from a typescript. In view of this, the price seems rather high. There are a number of misprints, and at times the author's style is a little garbled.

To sum up, this is a useful compilation of theoretical results on distribution theory and significance testing in multivariate analysis. It is quite comprehensive, but does not cover factor analysis.   J. F. SCOTT

CORRESPONDENCE

Forestry Policy

SIR,—Your petulant footnotes to Professor Wareing's letter (*Nature*, **241**, 414 ; 1973) are no more convincing than the assertions in your editorial that he so clearly corrected. On forest research there is one further point that needs to be made.. The service given to private forestry by the Forestry Commission's research programme, and by individual officers of the Research Division, is of immense value and has been a major factor in the achievement of the very high standard of management now existing in private woodlands. This Society would wish to see the Research Division strengthened rather than dismembered as you suggest.

It is not against the annual operating costs of the state forests that the forest research budget should be assessed, but against the total value of the productive woodlands of Great Britain, a figure in excess of £1,000 million ; on such an assessment the modest 0.1% spent on research is surely inadequate.

In your review of *Forestry Policy* in general your unquestioning acceptance of the figures produced by the anonymous team of Government economists, and their theoretical basis, is worrying. Both have been shown to be unsound (*Quart. J. Forestry*, **66**, No. 4) and further evidence is accumulating of much available information having been omitted, which, among other things, reverses the costs to the exchequer of jobs in state forestry and in agriculture stated in paragraph 19 of the *Forestry Policy* paper, which you quote. There are other gross errors of assumption, much unrealistic oversimplification, and much defective deduction in the study, which explains why most of it was discarded by ministers in the paper.

You make reference to the agricultural policy of the European Community. I draw your attention first to the Mansholt Plan for Agriculture in the EEC, wherein it is proposed that more than 4 million hectares of agricultural land shall be forested ; secondly, to the draft EEC Directive on Forestry signed by the Council of Ministers on January 10, 1973, which details the measures by which this is to be brought about. These measures include: 70 to 90% subsidy for forestation of agricultural land ; 50 to 70% subsidy for increasing the productivity of existing woods and forests ; an additional annual grant, lasting for 5 to 12 years, for forestation of marginal agricultural land ; cancellation of all subsidies for conversion of woodland to agriculture.

You make no mention of the future needs of this country for timber and wood products. Yet both the rate of consumption, and the cost, continue to rise. In its weak commercial position it is doubtful whether this country can afford the projected level of import, even if the material is physically and politically available, which is also doubtful. Europe is a net importer of wood ; the nine EEC countries import 57% of their requirements. In these circumstances the continued expansion of the area of productive forest under sustained management in Great Britain is a prudent and sensible investment.

Your four-point plan for forestry reveals a distressing lack of first hand knowledge. Available literature, much of it free, and the *Guide Map to Your Forests* recently published by Bartholomew for the Forestry Commission which is on sale at booksellers, enable anyone to go and judge for themselves how imaginatively the recreational facilities of the forests are being developed. You will find too that the people who use them do so because of the trees, not in spite of them.

Your vision of the forests being exploited as recreational parks by private commercial organizations is a horrifying one. The attractions and advantages of a silvicultural setting for recreation are many and various ; one of the main ones is that the management is in the hands of ecologically trained foresters who love their trees, the land on which they grow, the wealth of wildlife they support, and can interpret their understanding and transmit their enthusiasm to visitors. They are also able to obtain a remarkable degree of local involvement, support, cooperation, and goodwill in developing the cultural potential of their forests, which surely would not be forthcoming under the system you advocate.

Selective planting has been standard silvicultural practice for many years, as has the encouragement of colonization by native species of the land within the forest judged too poor to plant, and of other areas deliberately left unplanted for that purpose.

A 3% return in terms of timber, with the added social benefits of providing rural employment, amenity, shelter, water and wildlife conservation, recreation, sport, the framework of new landscapes and the perpetuation of existing ones, a primary source of energy, and a form of land use integrated with agriculture, makes forestry one of the best forms of investment for the nation.

Yours faithfully,
P. F. GARTHWAITE
The Royal Forestry Society,
102 *High Street,*
Tring, Hertfordshire

Good Intentions

SIR,—It gives me no pleasure to criticize well-meaning colleagues for their good intentions regarding suffering mankind ("Vietnam Bombing," *Nature*, **241**, 487 ; 1973), but in politics as in science good intentions alone are not enough.

The notion was advanced that appeals for international morality and the adoption of moral postures by neutralist politicians would do good. What evidence is there to support this hypothesis? During this century two world organizations were established precisely in order to solve the world's many problems in a moral way ; let us not shrink from calculating the ratio of successes to failures. Let us also recall with painful nostalgia the politics of the 1930s ; then, our kindly, democratic politicians and their well-meaning supporters pursued their moral policies until the political nemesis of 1939 : then, distinguished neutralists including Roosevelt and Gandhi—and perhaps also a Scandinavian or two—scored full marks for pontification but zero for knowledge of, and interest in, the relevant power stakes ; then, those who bothered to deduce the counterproductivity of such high-minded naivety were abused as warmongers and worse.

If Dr Morten Simonsen is convinced by his historical analyses that preaching is the most effective method for realizing political ends, let him enlighten and convince us—with his examples. But if, like Henry Ford, he dismisses history as bunk, let him not wonder how such men as Talleyrand, Bismarck, Disraeli, Marx, Lenin, and even Kissinger successfully advanced their policies. Can anyone believe that the political wilderness would be more amenable to the moralism of contemporary political babes than it was at the time of the Children's Crusade?

Yours faithfully,
O. LL. LLOYD
8 *Suffolk Road,*
Edinburgh 9

The Burden of Proof

SIR,—The creationists writing in defence of their beliefs are on the wrong tack; no one disputes their right to any theory whatever. What most biologists of my acquaintance abhor are the recent steps three American states have taken to interfere with biology teaching. California, for example, now includes in its guidelines to publishers of school and college texts a statement ("some of the scientific data may be best explained by a creation theory") with which few biologists agree.

The conscientious and informed teacher will ride the blow easily. It is, after all, good teaching if alternative ideas on the origin of species are briefly discussed and rationally dismissed. The teacher should be relating evidence to theory rather than handing out facts. What is unfortunate is that some teachers may be affected by the legislation and will not appreciate the weighting that a specialist in evolution would accord conflicting theories. Modern disciplines depend on the establishment of books, individuals and schools as "authorities". Once such an authority has been set up it is reasonable that conflicting theories gather their evidence and appear as challengers. The workers in the field will then judge the evidence and predictions of the competing ideas. Evolution itself has appeared as a challenger and passed the test while creationism has been demoted; defeated challengers are entitled to retain their views and to search for new evidence but not to pretend to authority. The burden of proof rests with the creationists.

A number of creationists[1-3] have written vaguely of "flaws" and "unanswered questions" in evolutionary thought. Such as? Even if there are any, this alone is not enough: creationism must be seen to be a better fit to the data. Only two arguments have been specifically mentioned. One is novel[4], albeit facetious. This cites some recent attempts[5] to quantify the role of genetic drift in evolution. Apart from the fact that this role is still contentious itself, evolution by drift is still evolution and not creation. Several creationists try to explain away the fossil record by postulating a succession of creations[3,6,7]. This raises a multitude of unanswered questions. How many creations? How often? Why a plurality? Why so many clearly marked trends in fossil series? and so on.

Why do many of *Nature*'s correspondents accept the Bible as the ultimate "authority" for the creation theory? This is not only poor biology but poor creationism too, for any archaeologist, theologian or philosopher could tell them that many of the stories in the Bible are copied from the folk-tales of long-ago tribes more ancient than the Hebrews[8].

Yours faithfully,

J. P. A. ANGSEESING

Saint Paul's College,
Cheltenham GL50 4AZ

1 Van Kley, H., *Nature*, **240**, 265 (1972).
2 Allbrook, D., *Nature*, **241**, 150 (1973).
3 Hayward, A. T. J., *Nature*, **240**, 577 (1972).
4 Harkins, R. N., Stenzel, P., and Black, J. A., *Nature*, **241**, 226 (1973).
5 Haigh, J., and Smith, J. M., *Genet. Res.*, **19**, 73 (1972).
6 Lucas, E. C., *Nature*, **240**, 366 (1972).
7 Fairbairn, J. W., *Nature*, **241**, 225 (1973).
8 Cleator, P. E., *Lost Languages* (New American Library, 1962).

Environmental Education

SIR,—This Institution is now carrying out a survey of current and anticipated provisions at establishments of higher and further education and at schools in the field of education in environmental subjects. A substantial proportion of these establishments have already replied and the information supplied is now being analysed.

May I approach, through the courtesy of your columns, those interested in "environmental education" at various levels to submit private communications of relevance. The aim of this particular exercise is to sample intelligent public opinion outside the official institutions.

Yours faithfully,

J. ROSE

The Institution of Environmental Sciences,
14 Princes Gate,
Hyde Park, London SW7 1PU

In Defence of Dingle

SIR,—Well, physics can now rest easy, in the assurance that it has been saved from heresy. Not one, but two occasions have been found in *Nature* to put down Professor Dingle (*Nature*, **239**, 242; 1972; and **241**, 143; 1973). If people really thought that Dingle's work did not deserve serious thought and discussion, would it not have been better to ignore it completely?

When Dingle has failed to get a hearing, and his opponents seem to agree on little except the fact that they are opponents, it would be of little use for me to say anything on the matter as a piece of physics. But there are two or three general comments, which anyone might make, and which someone should make.

In the first place, Dingle was once recognized to be an authority in this matter. If he has now come to different conclusions, either there are good reasons for these second thoughts, or else they are to be put down as a foible of old age. But the writing is certainly not that of a senile man.

In the second place, it would appear that none of his critics has faced Dingle's points that (*a*) he was discussing physics, not mathematics; and (*b*) that all of the alleged experimental verifications involve circular arguments in their interpretation.

In the third place, if it should turn out that there is some truth in Dingle's views, the way in which they seem to have been brushed aside will not be likely to make science stand any higher in the public esteem. In the United States, especially, the "Velikovsky affair" left a bad taste in many mouths; it is surely not wise to seem to persecute another man, and one whose views are by no means so unorthodox.

Yours faithfully,

H. L. ARMSTRONG

Addendum

IN the article "The First Fossil Record of Caecilian Amphibians" by R. Estes and M. H. Wake (*Nature*, **239**, 228; 1972) the identification for Fig. 1 *k-o* was omitted from the figure legend. It should read: *k-o*, *Geotrypetes seraphinii*, MVZ 98253.

Announcements

International Meetings

March 22, **13th International Technical Scientific Meeting on Space** (Secretariat, Via Cresecenzio n.9, 00193 Roma).

March 26–30, **Annual Chemical Congress** (Dr J. F. Gibson, The Chemical Society, Burlington House, London W1).

March 27–29, **Ultrasonic Conference and Exhibition** (Ultrasonic International '73. IPC Science and Technology Press Ltd, IPC House, 32 High Street, Guildford, Surrey).

March 27–29, **PowTech International Powder Technology and Bulk Solids Exhibition and Conference** (Specialist Exhibitions Ltd, Green Dragon House, 64 High Street, Croydon, Surrey).

March 27–29, **The Practical Implications of Fracture Mechanisms** (Meetings Secretary, The Institution of Metallurgists, Northway House, London N20).

March 28, **Corrosion and Deterioration of Metals and Alternative Engineering Materials** (Assistant Secretary, 14 Belgrave Square, London SW1).

March 28–30, **Nuclear Structure and High Energy Physics.** (The Meetings Officer, The Institute of Physics, 47 Belgrave Square, London SW1).

March 29, **Rancidity in Fatty Foods** (Mr J. Watson-Walker, Symposium Secretary, Department of Chemistry, The University of Technology, Loughborough, Leicester).

March 29–31, **Tenth Symposium on Biomathematics and Computer Science in the Life Sciences** (Office of the Dean, The University of Texas Graduate School of Biomedical Sciences, Division of Continuing Education, PO Box 20367, Houston, Texas 77025).

March 29–31, **Archaeometry and Archaeological Prospection** (Mrs Romie Tiplady, Research Laboratory for Archaeology and the History of Art, 6 Keble Road, Oxford).

April 2–3, **Society for Electrochemistry, Spring Informal Discussion Meeting** (Dr J. E. B. Randles, Department of Chemistry, Haworth Building, The University of Birmingham, PO Box 363, Birmingham B15 2TT).

April 3–6, **Tenth International Mineral Processing Congress** (Imperial College, Exhibition Road, South Kensington, London SW7).

April 3–6, **Activated Carbon in Water Treatment** (The Water Research Association, Medmenham, Marlow, Buckinghamshire SL7 2HD).

April 3–13, **Education of Teachers for Integrated Science** (Science Teaching Center, University of Maryland, College Park, Maryland 20742 USA).

April 4, **New Techniques and Applications in Scanning Electron Microscopy** (Meetings Officer, The Institute of Physics, 47 Belgrave Square, London SW1X 8QX).

April 9–11, **Oligosaccharides** (Dr W. R. Williams, Chemistry Department, Birkbeck College, Malet Street, London WC1E 7HX).

April 9–11, **Seventh Thin Films Conference** (Meetings Officer, The Institute of Physics, 47 Belgrave Square, London SW1X 8QX).

April 9–12, **Cancer Detection and Prevention** (Secretary, Istituto Di Oncologia "F. Addari", Viale Ercolani 4/2 40138 Bologna, Italy).

April 10–13, **Fifth National Atomic and Molecular Physics Conference** (Institute of Physics, 47 Belgrave Square, London SW1X 8QX).

April 10–13, **Propagation of Radio Waves at Frequencies above 10 GHz** (Institute of Electrical and Electronics Engineers).

April 13, **Symposium on the Monitoring of Electron Capture Nuclides and Soft Beta Emitters** (J. R. A. Lakey, Publicity Secretary, British Radiological Protection Association, c/o Royal Naval College, Greenwich, London SE10).

April 15–19, **The "Sea Peoples"** (Professor R. A. Crossland, Department of Greek, The University, Sheffield S10 2TN).

April 15–19, **Industrial Aspects of Biochemistry** (The Secretariat, FEBS Special Meeting, IMA Conference Centre, 10 Fitzwilliam Place, Dublin 2, Ireland).

April 15–20, **57th Annual Meeting of the Federation of American Societies for Experimental Biology** (Mrs T. C. Heatwole, Director, 5110 West Franklyn Street, Richmond, Virginia 23226).

April 16, **Current Progress in Palaeobotany in Britain** (Dr Keith Allen, Department of Botany, The University, Bristol BS8 1UG).

April 16–18, **Liquid State** (Professor J. G. Powles, The Physics Laboratories, The University, Canterbury, Kent. Details also from Meetings Officer, The Institute of Physics, 47 Belgrave Square, London SW1X 8QX).

April 29–May 5, **Euchem Conference on Stereochemistry** (Professor R. H. Martin, Department de Chimie Organique, Universite Libre de Bruxelles, 50, Ave. F.-D. Roosevelt 1050 Bruxelles/Belgique).

April 30–May 1, **Electro-Optics Principles and Applications** (National Offices, PO Box 288, Redondo Beach, California 90277).

Reports and Publications

not included in the Monthly Books Supplement

Great Britain and Ireland

Coal and Energy Policy in Europe: a Report by the British Coal Industry. (Report issued jointly by the National Coal Board; British Association of Colliery Management; National Association of Colliery Overmen, Deputies and Shotfirers; National Union of Mineworkers; Institution of Mining Engineers.) Pp. 9. (London: National Coal Board, 1972.)   [1812

Royal Observatory Annals. No. 7: Photometric Standard Stars. By A. W. J. Cousins. Pp. 86. (Herstmonceux: Royal Greenwich Observatory, 1972.) £1.15 net.   [1812

The International Commission on Radiological Protection. ICRP Publication 19: The Metabolism of Compounds of Plutonium and other Actinides. (A Report prepared by a Task Group of Committee 2 of the ICRP.) Pp. 59. (Oxford and New York: Pergamon Press, 1972. Published for the ICRP.) £1.50.   [1812

Bulletin of the British Museum (Natural History). Zoology. Vol. 23, No. 3: The Gunong Benom Expedition 1967. 4. New Records of Malayan Bats, with Taxonomic Notes and the Description of a New *Pipistrellus*. By J. E. Hill. Pp. 21–42. 85p. Vol. 23, No. 9: The Gunong Benom Expedition 1967. 11. Notes on Zoogeography, Convergent Evolution and Taxonomy of Fleas (Siphonaptera), Based on Collections from Gunong Benom and Elsewhere in South-East Asia. 1. New Taxa (Pygiopsyllidae, Pygiopsyllinae). By R. Traub. Pp. 201–305 + 58 plates. £7.15. (London: British Museum (Natural History), 1972.)   [1812

Geological Survey of Ireland. Special Paper No. 2: Upper Old Red Sandstone and Lower Carboniferous of the Slieve Beagh Syncline and Its Setting in the Northwest Carboniferous Basin, Ireland. By D. Sheridan. Pp. vi + 129 + plates 10–21. (Dublin: Geological Survey Office, 1972.)   [1812

Toxicological and Environmental Chemistry Reviews, Vol. 1, Numbers 1/2, June 1972. Edited by Roland W. Frei and Otto Hutzinger. Subscription Rates (per volume postpaid). 4 issues per volume. Great Britain: Libraries £17.25; individuals who warrant the journal is for their own use and order direct from the publisher, £5.15. USA/elsewhere: Libraries $45/£18.75. Individuals who warrant the journal is for their own use and order direct from the publisher, $16/£6.65. (London and New York: Gordon and Breach, Science Publishers, 1972.) [1812

Department of the Environment ; Scottish Office. Committee on the Rating of Plant and Machinery—Report. Pp. iv + 26. (London: HMSO, 1972.) 26p net.   [1812

Biochemical Education, Vol. 1, No. 1, Autumn 1972. (A Quarterly Bulletin of the International Union of Biochemistry.) Pp. 1–16. Subscription: £2; $6 for 4 issues. (Leeds. Biochemical Education. Department of Biochemistry, 9 Hyde Terrace, 1972.)   [1912

The University of Hull. Annual Report of the Council and the Senate to the University Court, 1971/1972. Pp. 179. (Hull: The University, 1972.)   [2012

The Orthopaedically Handicapped Child: Social, Emotional and Educational Adjustment—An Annotated Bibliography. By Doria Pilling. Pp. 56. (Windsor: National Foundation for Educational Research, Book Division, 2 Jennings Buildings, Thames Avenue, 1972.) £1.20.   [2012

Greater London Council Scientific Branch. Annual Report of the Scientific Adviser 1971. Pp. 115. (London: Greater London Council, 1972) £2. [2112

Department of the Environment. The Welsh Office. Report of a River Pollution Survey of England and Wales. Volume 2: Discharges and Forecasts of Improvement. Pp. xiii–231. (London. HMSO, 1972.) £4.60 net.   [2112

Department of Education and Science Sources of Information on European Organisations Pp v+22 (London: Department of Education and Science, 1972.)   [2112

Bulletin of the British Museum (Natural History). Entomology. Vol. 27, No. 7: Contributions Towards a Revision of *Myrsidea* Waterston. VII. (Phthiraptera: Amblycera: Menoponidae.) By B. K. Tandan. Pp. 369–410 + 2 plates. (London: British Museum (Natural History), 1972.) £1.95   [2112

Some Aspects of Process Licensing in the Fertiliser Industry. By J. D. C. Hemsley. Pp. 15. (London: The Fertiliser Society, 1972.)   [2112

Ministry of Posts and Telecommunications. Report of the Television Advisory Committee. Pp 21. (London: HMSO, 1972.) 14½p net.   [2112

Nuclear Enterprises. 1972 Scintillator Catalogue. Pp. 28. (Edinburgh: Nuclear Enterprises. Ltd., Sighthill, 1972.)   [2712

Laboratory Report on Biological Transmutation. By Dr D. B. Long. Pp. 20. (Braintree, Essex: Henry Doubleday Research Association, 20 Convent Lane, Bocking, 1972.) 20p.   [2812

The Royal Society. Scientific Research in Schools Committee—Report to Council 1972. Pp 20. (London: The Royal Society, 1972.)   [2812

Centre for Environmental Studies. 1 fth Annual Report, April 1971 to March 1972. Pp 57. (London: Centre for Environmental Studies, 1972.) [2912

Kent Instruments and the Metallurgical Industry. Pp. 22. (Luton, Bedfordshire: Kent Instruments Limited, 1972.)   [2912

Hydrogen Thyratrons—Preamble. Pp. 50. Storage Tubes—Preamble. Pp. 24. (Chelmsford, Essex English Electric Valve Co., Ltd., 1972) Gratis [11

Forestry Commission. Fifty-second Annual Report and Accounts, 1971–72. Pp. 102 (8 plates). 75p Report on Forest Research 1972. Pp. vii + 193 + 10 plates. £1.60 net. Forest Record No. 84: Winter Temperatures and Survival of the Green Spruce Aphid. By C. I. Carter. Pp 10. 7p (London: HMSO, 1972.)   [21

Department of the Environment. Welsh Office. Rate Rebates in England and Wales, 1971–72 Pp. 65. (London: HMSO, 1972.) 82p net.   31

British Medical Bulletin, Vol 29, No 1, January 1973: Symposium on Biological Basis of Radiotherapy. Pp. 1–90. (London: The British Council, 1973.) UK £2.25 ; other countries £2.50.   [31

Understanding the City of the Future By A. G Wilson. (Reprinted from The University of Leeds Review, Vol. 15, No. 1.) Pp. 32. (Leeds: The University, 1972.)   [41

The Scientific Proceedings of the Royal Dublin Society. Series A. Vol. 4, No 16: Ascomycetes of Oak Park, Co. Carlow, Ireland. By O. D. MacGarvie. Pp. 219–230. 40p. Vol. 4, No 17: The Silurian of the Croagh Patrick Range, Co Mayo. By M. J. Bickle, R. G. W. Kidd and Euan Nisbet Pp. 231 250 + plate 10. 75p. Vol. 4, No. 18: Award of the Boyle Medal to John Lighton Synge, F R.S Pp 251–252. 10p. Vol. 4, No. 19: Geometry and Physics. By J. L. Synge. (Boyle Medal Lecture.) Pp. 253–274. 75p. Vol. 4, No. 20: Artificial Key for the Identification of the Inflorescence Phase of Irish Grasses. By M. A. Farragher. Pp. 275–294 + plates 11 and 12. £1. Vol. 4, No. 21: Poaceae – Irish Members. Part 2: Artificial Key for the Identification of the Vegetative Phase of Irish Grasses By M. A. Farragher. Pp. 295–304 + plate 13. £1 Series B. Vol. 3, No. 9: Counts of Infective Units of the Take-All Fungus in Co. Donegal Oat Soils By M. J. Downes. Pp. 119–126. 35p. (Dublin: Royal Dublin Society, 1972.)   [41

Geological Excursion Guide to the Assynt District of Sutherland. By M. MacGregor and J. Phemister. Third edition, with an Appendix by M. R. W. Johnson. Pp. 68. (Edinburgh: Edinburgh Geological Society, 1972.) 60p.   [51

Bulletin of the British Museum (Natural History). Geology. Vol. 22, No. 2: Llandovery Conodonts from the Welsh Borderland. By R. J. Aldridge. Pp. 125–231 + 9 plates. (London: British Museum (Natural History), 1972.) £4.45.   [51

Ion Exchange and Membranes. Science and Technology of Dynamic Macromolecules, Vol. 1, No 1, August 1972. Edited by J. A. Mikes. Pp. 1-72. Subscription rates (per volume post paid) 4 issues per volume: Libraries and Institutions, USA/elsewhere $45; £18.75; Great Britain £17.25. Individuals (who warrant the journal is for their own use and order direct from the publishers), USA elsewhere $16: £6.65; Great Britain £5.15. (London and New York: Gordon and Breach Science Publishers, 1972.)   [51

Other Countries

Fisheries Research Board of Canada. Technical Report No. 329: Investigations into the Effects on Lobsters of Raking Irish Moss, 1970-1971. By D. J. Scarratt. Pp. 34. (St. Andrews, NB: Fisheries Research Board of Canada, Biological Station, 1972.) [1912

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Separation and Purification Methods, Vol. 1, No. 1, 1972. Edited by Edmond S. Perry and Carel J. van Oss. Pp. 1-236. Subscription rate: $19.50 per volume, 2 issues. Charge per volume for postage outside the US and Canada $1.50. (New York: Marcel Dekker, Inc., 1972.) [1912

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Gouvernement du Quebec. Le Conseil des Recherches Agricoles. Recherches Agronomiques—Sommaire des Resultats 1970/1971. (No. 16.) Pp. 151. (Quebec: Ministère de l'Agriculture et de la Colonisation, 1972.) [2012

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United States Department of the Interior: Geological Survey. Professional Paper 707: Interpretation of an Aeromagnetic Survey of the Amchitka Island Area, Alaska. By G. D. Bath, W. J. Carr, L. M. Gard, Jr., and W. D. Quinlivan. Pp. iv+25. (Washington, DC: Government Printing Office, 1972.) [2112

Smithsonian Contributions to Zoology. No. 129: Two New Species and a New Subgenus of Lucinidae (Mollusca: Bivalvia), with Notes on Certain Aspects of Lucinid Phylogeny. By Joseph C. Britton, Jr. Pp. 19. 35 cents. No. 131: Two New Caridean Shrimps, One Representing a New Family, from Marine Pools on Ascension Island (Crustacea: Decapoda: Natantia). By Fenner A. Chace, Jr., and Raymond B. Manning. Pp. 18. 30 cents. (Washington, DC: Smithsonian Institution Press, 1972. For sale by US Government Printing Office.) [2112

United States Department of the Interior: Geological Survey. Water-Supply Paper 2135: Surface Water Supply of the United States 1966-70. Part 14: Pacific Slope Basins in Oregon and Lower Columbia River Basin. Prepared in co-operation with the States of Oregon and Washington and with other agencies. Pp. x+1036. (Washington, DC: Government Printing Office, 1972.) $4.25. [2712

Carnegie Institution. Annual Report of the Director of the Department of Terrestrial Magnetism, 1971-1972. (Reprinted from *Carnegie Institution Yearbook 71*, for the year July 1, 1971-June 30, 1972.) Pp. 215-341. (Washington, DC: Carnegie Institution, 1972.) [2712

Institutt for Atomenergi, Kjeller, Norway. Kjeller Report No. 147: Ramona II—a Fortran Code for Transient Analysis of Boiling Water Reactors. By R. Holt and J. Rasmussen. Pp. iv+120+appendix. (Kjeller, Norway: Institutt for Atomenergi, Kjeller Research Establishment, 1972.) [2812

US Department of the Interior: Geological Survey. Bulletin 1345: Precambrian Rocks in the Cordes Area, Yavapai County, Arizona. By C. A. Anderson. Pp. iv+36+2 plates. (Washington, DC: Government Printing Office, 1972.) [2912

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Yet Another Lame Duck Survives

THE British government's conversion to the principle that an industry in trouble should have support from public funds is now almost complete, but the Conservative government seems to be no clearer than its Labour predecessor about the reasons for its generosity. Early this week, Mr Christopher Chataway, the Minister for Industry, announced that the government is to invest £4.9 million in a new company formed from the Norton-Villiers Division of Manganese Bronze Holdings Limited and Birmingham Small Arms Limited with the objective of manufacturing motor cycles. The need for this investment has come about because the Birmingham Small Arms company, which has long since exchanged its manufacture of rifles and other military weapons for the outwardly pacific but hardly less offensive trade of manufacturing motor cycles, has had two disastrous years in a row and has reached the point of collapse. The Norton-Villiers organization, by contrast, has been relatively successful in the past few years, recovering slowly but steadily from the collapse of its American market when, apparently to everybody's surprise, Japanese motor cycle manufacturers began selling motor cycles with large engines which were technically superior to those of their British competitors. What Mr Chataway said this week is that the government's investment in the new company is intended to secure an export market that could be worth £30 million a year in the decade ahead.

Several questions need urgently to be asked of the government. First, if the export of motor cycles is considered to be strategically necessary—and there is room for argument about that—might it not have been better that the public money now committed should have been invested in the successful company and not in its amalgamation with the unsuccessful company? No doubt the government is anxious to avoid the loss of jobs that would result from the complete collapse of BSA, given the several frights about the level of unemployment received last winter, but on this occasion it need not have worried. An investment in the successful company would surely have meant that the relevant parts of BSA, and the workers concerned, would have been snapped up. As things are, the shareholders, the management and the labour force of BSA will be protected from the knowledge that they have failed. And the government will have lost yet another chance of making good its persistent failure to recognize, in the recent history of public investment in British industry, that it is better to invest in successful enterprises than Mr John Davies's now proverbial lame ducks.

The second question, on which both the Labour and Conservative governments have been repeatedly caught out, is whether the new enterprise will be viable even with the government investment and the £10 million which it is hoped that the banks will now lend. For there is no secret behind the success of Japanese motor cycle manufacturers in the American market in the past few years. By the use of multi-cylinder engines, overhead camshafts

and such devices as electric starting motors, they have been able to sell products which are in many ways superior to those of British manufacturers. In the years ahead, the technical competition is likely to be still fiercer. It cannot be long before Japanese manufacturers are marketing machines which use rotary engines. It is vitally important to know whether the new company now put together will be able to suport research and development on the scale necessary to make it competitive in the 1980s. If it cannot, the outcome could be yet another failure in the not too distant future.

Yet another question which the government must answer is whether investment in motor cycle manufacturing is strategically worthwhile. It is not, after all, as if Britain is starved of opportunities for industrial investment. Indeed, there are several other ways in which an export business in less marginal products than motor cycles might be built up. To be sure, the government is worried about employment, while its hands are to some extent tied by the inflexibility of the British labour force. People brought up to manufacture motor cycles seem slow to recognize that they can just as well help to manufacture other kinds of industrial products, not merely motor cars but vacuum cleaners, refrigerators and the like. That said, however, there is also an urgent need for a re-examination of the government's plans for industrial retraining. Is it not high time that more efficient machinery for converting people to technologically advanced work was implemented? It could easily turn out, on a narrow accounting basis, that Britain would get better value for the money the government is now proposing to invest in making motor cycles by using it, instead, for sensible training programmes. In the long run, however, the only sustainable objective is that there should be a programme for the development of British industry which will provide not merely a skilled and adaptable labour force but a coherent strategy for deciding what should be manufactured. There is nothing wrong with the mechanism which exists already by means of which commercial institutions decide whether or not to risk money in new enterprises. The government's intervention, in the BSA case as well as in the rescue of other lame ducks in recent months, has blunted this machinery.

Princeton in Trouble

THE Institute of Advanced Study at Princeton is one of the most distinguished of all academic institutions in the western world. The tiny faculty of twenty-six has been able to exercise a profound influence on the development of scholarship, partly because of the quality of its members (including Einstein, von Neumann and Oppenheimer) and partly because of the historical accident that the institute functioned, in the 1930s, as a splendid

channel for preserving and transporting to the New World the academic traditions of Western Europe, Germany in particular. Since then, the institute has been a powerful stimulus for research in mathematics and the physical sciences and, though it has no formal connexions with undergraduate teaching institutions, the steady stream of visiting fellows through Princeton has helped enormously to enliven universities in the United States. In other words, the Institute of Advanced Study has been, for forty years or more, a powerful demonstration that ivory towers can still function efficiently. It is therefore a great misfortune that it should now be embroiled in an academic quarrel which, if the faculty does not watch its step in the next few weeks, could easily undermine much of what has been accomplished in the past forty years.

The facts are these. Dr Carl Kaysen, who succeeded Oppenheimer as director in 1967, has let it be known from the start that he would add a social science faculty to the three which have been there from the beginning— mathematics, physics and history. In 1970, Professor Clifford Geertz of the University of Chicago was appointed as the first tenured member of a social sciences faculty, apparently without dissent. More recently, there has been argument about the appointment of Dr Robert N. Bellah, a sociologist from Berkeley, to the same faculty. Dr Bellah is a specialist in the influence of religious symbolism on social structures. His proposed appointment to the faculty, advocated by Kaysen and Geertz, was considered by the combined faculty of the institute on January 15 and voted against by a margin of thirteen to eight. It seems to be agreed that while the recommendations of individual faculties of the institute on proposed internal appointments should be for all practical purposes mandatory, the faculty as a whole has only an advisory function in recommendations to appoint to newly established programmes such as that in the social sciences, which is why Dr Kaysen was within his rights in recommending to the trustees of the institute that Dr Bellah should be appointed. The outcome has, however, been unpleasant. For one thing, Dr Bellah's work is now being openly criticized by the faculty, many members of which are advocating a measure of faculty power that would give them ultimate responsibility for all tenured appointments. There is also an undercurrent of complaint at Dr Kaysen's administration of the institute and a group of fourteen members of the faculty have asked that there should be an outside scrutiny of "the director's stewardship", as a result of which a panel of the trustees is planning to hear views on this controversial subject this Saturday, March 24. Nobody would be surprised, but most people would be disconsolate, if the outcome were, now or at some time in the future, the director's resignation.

This is why it is important that there should be a better sense of moderation in this kind of academic community. Whatever the merits or defects of Dr Bellah's scholarship, it is absurd for anybody at Princeton to suggest that a single appointment can entirely change the character of the faculty. Of that there can be no dispute. Good institutions are precisely those which should be able to accommodate unevenness. The central issue is whether a faculty of twenty-six (enlarged to twenty-seven by Dr Bellah's presence) should have the close degree of control over all academic appointments which the dissidents at Princeton seem to want. It is hard to avoid the impression

that there is an element of dissent from Dr Kaysen's plan for a social science programme in what the dissident members of the faculty have been saying. For several years, the new director has not troubled to conceal his impatience with the narrowness of the institute's chief lines of inquiry, and it is entirely proper that if a new faculty is to be created in the social sciences, he should have an important say in its composition. From the outside at least, what the faculty is asking for is a degree of control over academic innovation which is in many ways intolerant. Unless the dissident members are somehow able to make their arguments less pernicious, they will find that they have done more damage to the institution they say they wish to defend than any number of unsatisfactory appointments might accomplish.

SURVIVAL OF THE FITTEST

THE doctrine of the "survival of the fittest" must be strangely understood in some quarters. The American papers report Prof. Agassiz as having expressed himself in this wise at a recent meeting of the Massachusetts State Board of Agriculture, of which he is a member :—" I do not know how animals originated ; a brilliant imagination that of Darwin ; a very necessary faculty in the scientist. The sense I know too well to misquote him. Hasty generalising of observation is Darwin all over. Natural selection is out of generation. Natural necessity, what is it ? Do we find that only the strong beget families ? *Observe plants at the foot of the White mountains, where are large trees, and so up to the summit, where they are mere shrubs.* The weak may and do survive as well as the strong. Ignorance lies at the base of the discussion."

Probably no one naturalist, however eminent, can be expected to know everything, or even all simple things. Can it be possible that Prof. Agassiz supposes (as his argument seems to require) that the dwarf trees in question grow and survive near the top of the mountain, *notwithstanding* they are not the fittest, rather than *because* they are the fittest, for the conditions ? And does he conceive the doctrine of natural selection to be founded upon some idea of an abstract fitness, irrespective of the conditions, and not upon the survival of the fittest under and in consequence of the conditions ? Surely the argument brought against the doctrine is a good illustration in its favour, only an extremely simple and elementary one.

We never could quite comprehend why Prof. Agassiz should give himself so heartily and persistently to the work of demolishing the doctrine of the derivation of species, in all its forms, considering how large and honourable a part he has himself taken in laying the foundation upon which the modern doctrine has been built. Of these foundations none is stronger than the capital one, generally supposed to be established by him, that the succession of species in time corresponds mainly with that in systematic rank, and is also somehow paralleled in the development of each individual of the higher ranks. So that, in view of his continued but unsuccessful efforts to drive the incoming doctrine out of the land, we could imagine him addressing his own important discoveries in the words used by Balak to Balaam : —" What hast thou done unto me ? I took thee to curse mine enemies, and behold, thou hast blessed them altogether."

From Nature, **7**, 404, *March* 27, 1873.

OLD WORLD

End of the Road in Sight for Nina

NINA, the 5GeV electron accelerator at the Daresbury Nuclear Physics Laboratory will have to be closed, probably in five years time. It has been realized for a long time that in order to keep the Science Research Council's spending on nuclear physics constant, either Nina or Nimrod, the 7GeV proton synchrotron at the Rutherford Laboratory, would have to stop operating when the 300 GeV accelerator at CERN became fully commissioned.

The announcement that Nina is to be scrapped was made by Sir Brian Flowers last week at the University of Newcastle. But this does not ensure the future of Nimrod for an indeterminate period for, apart from other considerations, the machine will be seriously outdated by the end of the 1970s.

The future of both high and low energy nuclear physics research in Britain for the second half of the 1970s is now taking shape. On the low energy front the Science Research Council's request for money to build a Nuclear Structure Facility is still with the Department of Education and Science and it looks very much as if the facility will now be built at Daresbury if the government approves the expenditure of £4 million over 5 years. High energy physics will be centred in Geneva with the 300 GeV accelerator while Nimrod will be used as a valuable back-up machine until it is probably phased out at the end of the decade.

But nuclear physics did not occupy all of Sir Brian's speech and his theme was what the chairman of the Science Research Council can and cannot do. In a frank revelation of the chairman's decision making powers, Sir Brian, in his last few months at the council before he becomes rector of Imperial College, covered most of the major decisions made during his tenure of office.

Sir Brian gave a detailed account of the series of decisions that culminated, eventually, in the British government agreeing to participate in building the 300GeV accelerator at CERN. He also gave a similar account of the not so successful attempt by the Science Research Council to persuade the government to provide money to build a high flux beam reactor in Britain. Sir Brian, modestly, pointed out how astrophysics research at the Culham Laboratory was taken over by the SRC from the United Kingdom Atomic Energy Authority and how, diplomatically, the rival claims of Sir Martin Ryle and Sir Bernard Lovell

Professor Sir Brian Flowers, Chairman, Science Research Council.

in 1968 for money to build respectively, a radio telescope at Cambridge, for £2 million and a giant new dish at Manchester for £5 million, were resolved in Sir Martin's favour. But there was a

consolation for Sir Bernard in money granted to improve the telescope at Jodrell Bank. Now, of course, it is Sir Bernard's turn. The Cambridge radio telescope is operational and plans are well advanced to build a new telescope in mid-Wales for the University of Manchester Nuffield Radio Astronomy Laboratory.

Sir Brian also pointed out how the attempts of the Science Research Council to shift the balance in post graduate training from science to engineering is being frustrated by the universities. During the past few years the SRC—as a matter of national policy, says Sir Brian—has been transferring its studentships from science to engineering, but the universities with equal vigour have been transferring the studentships not under the control of the SRC from engineering to science. This, says Sir Brian, is one of the "principles of frustration" arising from the dual support system and demonstrates how the power of a research council is limited by its abilities to persuade. So postgraduate engineering training has increased at a much slower rate than the SRC wanted it to and postgraduate

SOVIET SCIENCE

Planetokhods Planned

from our Soviet Correspondent

As Lunokhod-2 continues its successful programme of investigations in *Mare Serenitatis*, an interview in *Pravda* with Academician A. A. Blagonravov suggests that plans are already being made in the Soviet space programme for the automatic exploration of the planets by similar travelling laboratories. Although some of his remarks relating to the possible "planetokhod" exploration of Venus and the outer planets seem highly speculative, the possibility of a "Marsokhod" seems to have reached the stage of constructive planning.

The principal difference between the lunokhods and the projected Mars vehicle would be in the manner of control. The lunokhods are controlled from Earth—a Mars vehicle would have to be self-controlling at least as far as such vital commands relating to its motion as "start" and "stop" are concerned. Certain instrument units would also have to be autonomic, in order to investigate immediately any specific feature encountered during motion. Academician Blagonravov does not,

however, speak of a fully automatic vehicle, and it would appear that there would be some Earth control—perhaps in the activation of data transmission sequences.

The Marsokhod plans are concentrating on increasing the distances the vehicle can travel quickly rather than on extending its life span. This seems to have been dictated by communications considerations—a rapid, productive survey close to conjunction being preferable to the slow, long-term surveys carried out by the lunokhods.

The Martian atmosphere is envisaged as presenting "difficulties" for such a vehicle, and special protection will have to be included against dust penetration and friction of the moving parts. This, however, is essentially a matter of modifying the vehicle itself and its external sensors, since the instrument units proper operate in a sealed compartment with pressure and temperature close to Earth-normal. In Academician Blagonravov's view, the lunokhods may be considered as prototypes for future Mars craft, and the successful landing of a Marsokhod on Mars itself in the "fairly close future", he says, "cannot be doubted".

science training is still being maintained at a level that is diffiult to justify at present.

In spite of this condemnation of the principle of dual support Sir Brian says that it is important that the universities be not wholly reliant on the research councils for support for their research. The SRC is perfectly right "to decide that it can only afford to support (say) five major university centres in a given topic," said Sir Brian "or to support only (say) 20 postgraduate schools of chemistry and to let the rest go hang". Then universities which were really determined "to achieve greatness" could spend their own money to achieve it and become one of the accepted universities at the expense of one of the others already on the list.

NUCLEAR POWER

Plans for the Future

By 1985 it is planned that 33 per cent of the electricity generated within the European Economic Community will arise from nuclear reactors. The European Commission recently approved a plan that sets as an objective a minimum output of 100,000MWe from nuclear power plants by the mid-1980s which will amount to ten per cent of the total energy needs (including oil and gas) of the community at that time.

At present the total community nuclear power capacity is 5,500MWe of which 3,250MWe are generated in England and Wales by the Central Electricity Generating Board. If plants under construction are taken into consideration the total community output in 1975 will be 12,000MWe and about 23,500MWe in 1977. In Britain five Advanced Gas Cooled Reactors are being built with a total capacity of about 6,500MWe which will be operational by 1980. These reactors are of course the first AGRs to be built.

The total electricity output in England and Wales is 56,000MWe at present which is projected to rise to 160,000 MWe by the end of the century. The CEGB estimates that one half of this will be produced by nuclear power.

If the European Commission's objective of 100,000MWe output from nuclear power in 1985 is to be realised then 45,000MWe should be produced by 1980. This, according to the community's Nuclear Information Programme, implies that 7,000MWe a year have to be added between now and 1975 and 11,000MWe to 12,000MWe a year between 1976 and 1980.

On a longer time scale the Nuclear Information Programme estimates that in 1990 the nuclear power output of the community should be 210,000MWe and 620,000MWe in 2,000.

But the community is not completely

ignoring the claims made by the coal industry for coal to be given its place in the energy equation. The European Commission has already issued a draft of its scheme for aiding the iron and steel industry within the community in buying coking coal and cokes. This draft is now before the Council of Ministers awaiting approval.

The British Coal Industry will no doubt welcome the community's interest in coal. When Britain joined the EEC in January the community's coal output increased from 170 million to 300 million tons a year. Late last year (see Nature, 240, 516 ; 1972) a document, Coal and Energy Policy in Europe, was produced by the National Coal Board, the National Union of Miners and other bodies which called for coal to be used to "its full and effective potential" within the European Community. This report pointed out that by 1980 there will be a gap between the energy produced within the community by natural gas, north sea oil, lignite, nuclear power and hydrolectricity, and the requirements at that time. This gap, which the report estimates to be almost 1,200 million tonnes of coal equivalent, will be filled by coal and imported oil. The plea of the British report was that "as large a part of this market as possible be supplied with coal".

VIVISECTION

Fund for Research

A FUND to encourage research techniques that do not involve vivisection has been set up. Following a two-day seminar held in London last week on the potential of humane non-animal research techniques, the National Anti-Vivisection Society announced that it was providing £10,000 to start the fund.

Known as the "Air Chief Marshal the Lord Dowding Fund for Humane Research", the fund will provide prizes or grants for scientists carrying out research "likely to lead to the alleviation of human or animal suffering, or likely to lead to the advancement of a new discovery which shall be useful for saving or prolonging life". The only caveats are that live animals must not be involved in the experiment at any stage, and applicants must not hold a licence for animal experimentation.

Mr Richard Body, MP, Vice-Chairman of the All-Party Parliamentary Humane Research Group, said that "we hope the grants will also encourage scientists to seek means of evaluating new drugs and medicines without resort to tests on live animals. Quite apart from the suffering inflicted on many of the 5.5 million animals now used annually in experiments in the United Kingdom the use of animal tests for the evaluation of new drugs is so unreliable in many respects that unless

more efficient methods are found many doctors and scientists fear we could be heading for another tragedy on the thalidomide scale".

CONSERVATION

Whale Imports Banned

THE British government has banned the import of the majority of whale products. The ban, which came into effect at midnight on March 15, comes after considerable pressure by environmental groups to get Britain to suit its actions to its words.

Britain has not been an active whaling nation since 1963 and is one of the nations that has supported moves within the International Whaling Commission to cut the whale catch substantially as it has become plain that many species of whales have been overhunted. But, while Britain has argued that whaling should be controlled, whale product imports have gone ahead unfettered.

But last week's ban is not a total one. Mr Anthony Stodart, Minister of State, Department of Agriculture, Fisheries and Foods, announce that the Department of Trade and Industry's studies on alternatives to the use of whale products have shown that some industries can use substitutes for sperm oil but that others will have difficulty finding replacements. The decision, therefore, is to ban the use of all whale products except sperm whale oil used as engine lubricant, spermaceti wax, ambergris and whale products incorporated into manufactured products abroad and then imported.

Friends of the Earth, who have campaigned to prevent whale imports for more than a year now, are well pleased with the decision, although they are eager that the ban should be extended to cover sperm whale oil.

Nonetheless the government's action will produce a considerable reduction in whale product imports. Nineteen thousand tons of whale meat valued at £2.2 million were imported in 1970; by 1972 these figures had fallen to 8.8 thousand tons valued at £1 million. These imports are now banned. The import of whale oil, other than sperm whale oil, which is put at 850 tons last year is also banned.

Although sperm whale oil can still be imported the amounts entering the country have been diminishing over recent years. In 1972 only 7,600 tons were imported, a little over half the amount imported in 1970.

Studies of alternatives to sperm whale will continue, and Friends of the Earth hope to continue their campaign for the complete ban of whale product imports in June when the International Whaling Commission is again due to meet in London.

FORESTRY

Pesticides and Planes

from a Correspondent

AGRICULTURAL chemicals and agricultural aviation, their relevance to the management of forests and their use in the fight against pests and diseases of forest trees, was the theme of a recent symposium of the Agricultural Aviation Group of the Royal Aeronautical Society and the Society of Chemical Industry, Pesticides Group.

The section of the symposium devoted primarily to chemicals was aptly timed as its chairman, Mr D. Bevan (Forestry Commission), noted in his opening remarks. A recent Green Paper (*Forest Policy*, HMSO, June 1972) envisages a wider remit for the two million acres of state-owned forests in the United Kingdom than merely cellulose production. Conservation, wildlife management, amenity and recreation may be added responsibilities in future. These changes may eventually loosen the economic constraints which apply to the use of fertilizers and pesticides in Bristol forests, but Mr J. F. Morgan (Forestry Commission) concentrated his analysis on the potential for these chemicals on a continued need for them to pay for themselves by increased cellulose yield. Discounting their costs during the period of several decades which may elapse before the trees are felled, Mr Morgan showed that the required returns from chemicals can seldom be obtained in practice from cellulose production.

Two reports gave the latest information on the control of Dutch elm disease. Dr J. N. Gibbs (Forestry Commission) described 1972 trials with basal injections of a solution of benomyl directed against the causative fungus, *Ceratocystis ulmi*. He reported hopeful results and estimated that the treatment cost of about £10 per tree would be justified on some 370,000 of the 2.7 million large elms currently at risk in the southern half of England—justified in this case by their amenity value or the high cost of felling if they were allowed to die, and not by future timber production. Promising preliminary results with insecticides against the beetle vectors of the fungus were also reported by Mr T. M. Scott (Forestry Commission).

Two reviews dealt with the use of aircraft in forestry. After describing the situation in Europe, Dr W. J. Maan and C. H. Cottle (International Agricultural Aviation Centre) concluded that use of aerial fertilizers would become more frequent. Broad spectrum insecticides would be replaced by more specific compounds or biological control agents, but in Europe aerial pest and disease control would still be confined, for the most part, to situations where the

survival of the crop was threatened. Applications of herbicide would increase slightly and forest fires would continue to be spotted and occasionally fought from the air. This forecast seemed restricted when compared with the present situation in Canada, which was comprehensively reviewed by Professor P. H. Southwell (University of Guelph). He highlighted the divergence which has occurred in Canada between agricultural and forestry aviation, chiefly because forest spraying frequently involves uniform areas of terrain which require few turning points. Thus relatively fast and heavy ex-military aircraft are used with large payloads, achieving ten or twenty times the rate of work of agricultural operations. Ground-based fire spotting, the meeting was told, has been almost superseded in Canada by airborne infrared patrol techniques and, once located, fires are eliminated or temporarily contained by aircraft.

BRITISH ASSOCIATION

Student Conference Plan

THE British Association is to hold a student conference in January 1974. The four-day meeting, from January 2 to 5, will be centred on the Royal Society and the subject will be the social responsibility of the scientist within the community.

The BA hopes that the conference—the first specifically for students — will form a springboard for its attempts to increase the number of students interested and involved in the association's activities.

In the past the association has woefully neglected the interests of its student membership, which, before last September's meeting in Leicester, numbered only 147. During the Leicester meeting the number of student members rose to more than 200 and the idea of a student conference emerged.

The programme will open with a meeting at the Royal Society which will be addressed by one of the society's officers. On the Thursday and Friday mornings two speakers will lecture during the morning and discussion groups will mull over the points raised in the afternoons. On the Friday evening it is hoped that the groups will report to the conference and discuss their findings with a panel of speakers.

Subjects to be covered include the impact of science and technology on society and the relative allocation of resources to different areas of science.

The British Association hopes that the conference will become a regular item on its agenda and to encourage as many students as possible to attend the association is to subsidize the conference in order to keep the cost for individual students down.

COMPUTERS

Anger at the End

INTERNATIONAL Computers Limited's managing director, Mr Geoffrey Cross, accused the Select Committee on Science and Technology of asking damaging questions in the closing minutes of the committee's inquiry into the computer industry last week.

Mr Ian Lloyd, a member of the committee, had asked Mr Cross and Mr Tom Hudson, ICL's chairman, if they had any comments on the committee's questions. Mr Cross promptly quoted an occasion when Mr Lloyd had asked Christopher Chataway, Minister for Industrial Development, if the £14.2 million the government has given ICL to support its new product range would be sufficient, the select committee having recommended that £50 million support should be given to the industry. This, Mr Cross said, could be damaging and it implied that the company had not got what it needed. In fact £14.2 million was the amount it had requested from the government.

Again, Mr Cross said that ICL had been asked whether it would rather merge with Univac or Nixdorf. "That's a damaging question," Mr Cross said, "because it assumes we'll do one or the other." Mr Cross emphasized that he had made these points to the committee during private session. Mr Airey Neave, the committee's chairman, was clearly annoyed at Mr Cross's action, warning him "to be very careful about what you say in public about private sessions", and suggesting that it was the answers to the questions that might be damaging rather than the questions themselves.

After the hearing Mr Neave made it clear that the private hearing had been at ICL's request, not at the committee's.

Mr Cross also described Mr Christopher Layton's claim that ICL could not survive without government support after 1976 to 1977 as "a lot of nonsense". He had, however, had a meeting with Mr Layton the previous week, and felt that his disagreements with Mr Layton were over matters of detail rather than over fundamentals.

Mr Hudson told the committee that at present the influence of the EEC commission on the computer industry was fairly small, but he admitted that this could change considerably in the "not too distant future" if the commission acquired funds for its ideas.

ICL told the committee that as yet it had not had any contact with the Department of Trade and Industry's computer requirements board which was set up at the end of 1972. The company also said that the British government was not an advanced user of computers and relied on them less than other European governments.

Knives Out for Surgeons

by our Washington Correspondent

AFTER a year of being thrust into the public spotlight and being debated in medical journals, newspapers and committee rooms on Capitol Hill, psychosurgery made its first appearance in court last week. Brought before a three-man panel of judges in Detroit, the court case is likely to have important implications for the future of psychosurgery in the United States and by the time it is finished it will probably have exposed a number of other issues as well. The appearance was at a pre-trial hearing, as a result of which the judges have now decided that the case is worthy of a full scale trial. It is set to open in Detroit on March 27, and will probably last for several weeks.

At the centre of the case are a 36-year-old alleged murderer and rapist who has spent the past 18 years in institutions for the criminally insane, and a team of doctors from the Lafayette Clinic, the highly respected psychiatric research centre attached to Wayne State University. The man, known in the court case as Mr L, was to have been the first patient to take part in a project at the clinic designed to provide experimental treatment for violent patients in state hospitals in Michigan, in the hope that they could be returned to society.

The patients, selected on the basis of several factors including their intelligence, length of stay in hospital and inability to respond to other forms of treatment, would have been given a choice between treatment with a drug known to have some side effects—including possible impotence — and psychosurgery, or they could have opted for neither. Mr L, after having been told the risks associated with either form of treatment, opted for psychosurgery—in this case, the destruction of a tiny portion of the brain with deeply implanted electrodes.

He was transferred to the Lafayette Clinic from Ionia State Hospital, but before the operation could take place Mr Gabe Kaimowitz, a civil rights lawyer, filed suit to try to stop it. The case hit the headlines in the Detroit papers, Mr Kaimowitz got an injunction, and the full hearing opened last week. In the meantime, however, the Michigan state government, which was to have funded the project, withdrew its support and so the case as such, no matter what the court decides, is already dead. The court is thus in effect being asked to rule on a number of ethical issues surrounding psychosurgery in particular, and experiments involving prisoners in general. Its decision is therefore likely to have widespread implications.

Psychosurgery has become a subject of public debate chiefly because of the crusading of Dr Peter R. Breggin, a novelist and psychiatrist attached to the Washington School of Psychiatry. Breggin last year put together a scathing attack on psychosurgery, documented with examples of cases in which it has damaged the intellect or other functioning of patients on whom it has been practised, and his paper was read into the Congressional Record. He has suggested that new techniques, such as the use of electrodes, ultrasonics, and the injection of butane gas to destroy tiny areas of the brain, are likely to usher in a new age of lobotomy, and he believes that all psychosurgery should be banned.

Although estimates vary widely, there are reckoned to be about 500 psychosurgery operations performed in the US each year on a variety of patients. Unlike the classical lobotomy operation, which reached its height of popularity in the 1950s and was used on up to 50,000 people in the US, psychosurgery now rarely involves actually cutting into the brain, but it does have one important facet in common with classical lobotomy—it is irreversible. Moreover, although the new techniques destroy less brain material, there is still no theoretical understanding of the function of the material which is destroyed.

Opponents of psychosurgery also point out that, unlike normal medical practice, the technique is designed to destroy tissue which is neither diseased nor malformed. Psychosurgery, which

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APPOINTMENTS

Two Down but More to Go

by our Washington Correspondent

ONE sign of the Nixon Administration's lack of enthusiasm for science and technology is the fact that key positions in the federal scientific bureaucracy have been unfilled for months. But at last a few appointments have been made. Last week, President Nixon announced that Dr Charles C. Edwards, now Commissioner of the Food and Drug Administration, has been nominated as Assistant Secretary for Health in the Department of Health, Education and Welfare—the top health position in the federal government—and that he has nominated Dr Betsy Ancker-Johnson, an engineer and consultant to Boeing, to be Assistant Secretary of Commerce for Science and Technology. The health job has been vacant since Dr Merlin K. DuVal resigned in December, while the Commerce job has been vacant since Dr James T. Wakelin jun. resigned in August last year. Both nominations must be confirmed by the Senate.

The elevation of Dr Edwards to the position of Assistant Secretary for Health has been expected for several weeks, and last week's announcement has been greeted with approval from most quarters. As commissioner of the FDA, it is generally considered that Dr Edwards did a good job in often extremely difficult circumstances. The FDA is constantly caught in the crossfire between a strong and increasingly more vocal consumer movement and the food and drug industry. Dr Edwards is, in fact, the only senior health official left in the Administration since President Nixon either accepted or forced the resignations of the Surgeon General, the Director of Health Services and Mental Health, the Assistant Secretary for Health and the Director of the National Institutes of Health, but his promotion now creates a vacancy at FDA. No successor has yet been announced, and Nixon said last week that the choice would be made by the new secretary of HEW, Caspar Weinberger. Since the FDA is likely to be broken up with the passage of legislation to create an independent Consumer Protection Agency, Weinberger may have some difficulty finding a good person for the job.

is designed to alter behaviour, is usually distinguished from the treatment of epilepsy and the removal of brain tumours, which, although they may involve the destruction of brain tissue, are performed to combat organic disease.

The debate about the ethical implications of psychosurgery which has been taking place in the US recently has been emotionally loaded, and a set of hearings held by Senator Edward Kennedy last month, as part of his investigation of human experimentation (see *Nature*, **242**, 152 ; 1973), provided an outlet for many of the arguments on both sides of the fence. A sober and carefully measured appraisal of the situation was, however, given by Dr Bertram Brown, Director of the National Institute of Mental Health.

Brown told the committee that he believes that knowledge of the brain is at present too limited to provide justification for psychosurgery. "My own view", he said, "is that more knowledge and more refined techniques would be needed before one could determine unequivocal clinical indications for psychosurgical intervention". When asked by Kennedy if he believes that psychosurgery is a valid technique for treating behaviour disorders, Brown replied "My answer is a crisp negative".

He went on to say that although the federal government cannot regulate the practice of surgery, the Department of Health, Education and Welfare has published a set of guidelines for any experiments involving human subjects. These embody the principles that the risks to the patient are outweighed by the benefits to him or by the importance of the knowledge to be gained, that the experiment should have been subjected to peer-review and that the patient should be completely informed of the risks and give his consent freely.

In the case being studied by the Detroit court, the project was subjected to two reviews, and Mr L and his parents gave their consent to the operation after being informed of the risks. But a central issue in the court case revolves around the question of whether a person involuntarily detained in a mental institution is in fact in a position to give his consent to treatment freely. That, of course, is an issue in all research involving prisoners of any kind.

NAS

Reorganization Begins

by our Washington Correspondent

THE National Academy of Sciences has begun to implement the scheme for reorganizing its operating arm, the National Research Council, that was agreed at the annual meeting last year

(see *Nature*, **237**, 6 ; 1972). It was announced last week that an Assembly on Behavioral and Social Sciences and a Commission on Natural Resources have been established, and that two more assemblies and four more councils will be established during the next few months. Dr Robert McCormick Adams, dean of the Division of Social Sciences at the University of Chicago, has been appointed as chairman of the Assembly of Behavioral and Social Sciences, and Dr Gordon J. F. Mac-Donald, of Dartmouth College, who was a member of the Council on Environmental Quality until late last year, will be the first chairman of the Commission on Natural Resources.

Set up by President Wilson in 1916, the National Research Council is the organization responsible for carrying out the studies contracted by the academy, and it is administered by the Council of the National Academy of Sciences. Its reports, which are reviewed by a committee of academy members, thus bear the prestige of the academy, although they are prepared by committees consisting of scientists drawn from the whole scientific community and they do not necessarily include academy members.

Organized at present along divisional lines which roughly correspond to the chief scientific disciplines, the NRC is increasingly being called upon to perform studies which include inputs from several disciplines, and the reorganization is designed to make it more responsive to such demands.

The plan is to set up two more assemblies—concerned with the life sciences and with the physical sciences and mathematics—which, together with the new Division on Behavioral and Social Sciences, will be concerned chiefly with the welfare of their component disciplines. They will, for example, be concerned with the preparation of such reports as the recent survey of physics. In addition, they will provide manpower to serve on committees set up to study problems undertaken by the commissions. Although ultimate authority for the work of the assemblies will rest in the council of the academy, each will be run by an executive committee composed chiefly of academy members.

The commissions, in addition to that on natural resources, will deal with human resources, peace and national security, international scientific affairs, and "technologies in large, complex social systems" such as transportation and urban development. At present, some 8,500 scientists serve on committees of the NRC, and a statement on the new reorganization suggests that steps are being taken to strengthen selection of committee members so that "potential sources of bias—

whether real or apparent—are not permitted to undermine the credibility of the advisory process".

The reorganization plan has been a long time in coming, for it was first proposed by NAS President Philip Handler soon after he took office in 1969. It has, however, been delayed by a dispute between the National Academy of Sciences and the National Academy of Engineering over governance of the NRC. Although the NRC is the operating arm of both academies, only the council of the NAS has formal control over the affairs of the NRC under the terms of its charter. The engineering academy is unhappy about such an arrangement, and from time to time there have been murmurings that it would sever its ties completely with the NAS. At present they are still together, but the arrangements announced last week do not provide for the NAE to have any more voice in the running of the NRC than it has had in the past.

HEALTH RESEARCH

More Polish Accord

by our Washington Correspondent

ANOTHER scientific agreement between the governments of the United States and Poland was signed last week. This time, the agreement concerned health matters —in particular, the sharing of information and the exchange of scientists working chiefly in nine areas of health research. Signed in Washington by Caspar Weinberger, Secretary of Health, Education and Welfare, and the Polish Minister for Health and Social Welfare, Dr Marian Sliwinski, the agreement supersedes a memorandum of understanding dating from 1962. That memorandum was limited to activities funded with US owned excess foreign currencies derived chiefly from the sale of agricultural products.

The new agreement relates specifically to cooperation in research into cancer, cardiovascular diseases, occupational health, maternal and child health, rehabilitation, neurologic diseases, metabolic and endocrine disturbances, transplantation and nephrology and models of health protection organizations. The United States and Poland signed an agreement last year for cooperation on general scientific research, and the National Science Foundation recently agreed to help finance the building of a centre for the study of astrophysics near Warsaw.

HEAO

Picking Up the Pieces

by our Washington Correspondent

DURING the past few weeks NASA officials have been quietly picking up some of the pieces of the High Energy Astronomy Observatory (HEAO) programme, which in January became a casualty of the Administration's drive to hold down federal expenditure. They have put together a plan to launch three small HEAO satellites with Atlas-Centaur rockets between 1977 and 1979, and to complete the programme with heavier satellites launched by the shuttle in the early 1980s. The emphasis in the first part of the revamped programme will be on X-ray studies.

The plan developed partly from a meeting, held shortly after the Office of Management and Budget killed the programme, of those who would have flown experiments on the original HEAO satellites. It has since been endorsed by the Space Science Board of the National Academy of Sciences. Although still rather tentative, the chief elements of the plan probably will not change much, but Dr John Naugle, Associate NASA Administrator for Space Science, said last week that the HEAO programme will remain suspended "for at least a year" while the details are settled.

As it now stands, the plan is for the first scaled-down HEAO satellite to do an X-ray survey, and for the second to study individual point sources of X-rays. The third satellite will carry gamma ray and cosmic ray detectors for a survey, and the shuttle-launched missions will carry the heavier gamma ray and cosmic ray experiments.

As originally planned, the HEAO programme would have consisted of two large satellites launched by Titan rockets in 1975 and 1977, followed by two more large satellites launched by the shuttle in the early 1980s. Each satellite would have carried a range of experiments to detect X-rays, gamma rays and cosmic rays, and each would have carried a scientific payload of about 12,000 pounds. In contrast, the Atlas-Centaur is capable of launching high energy astronomy satellites with a scientific payload of 2,800 pounds.

Why concentrate on X-ray studies for the scaled-down HEAO missions? Apart from the fact that most of the gamma ray and cosmic ray studies originally planned for the programme are too heavy to be launched by the Atlas-Centaur, it is felt that the results from the first Small Astronomy Satellite, Uhuru, which was launched in 1971, provide a good base on which to build. Moreover, the follow-up to Uhuru, SAS-C, which is now scheduled for launch in 1975, should provide even more exciting results as a curtain-raiser

to the scaled-down HEAO mission. As Dr Robert Halpern, Programme Manager of HEAO, said last week, "We know we have something to grab hold of, the other two fields have promise, but it's just that—promise".

X-ray astronomers are, understandably, relatively pleased by the plan to concentrate initially on their subject. Dr Herbert Friedman, of the Naval Research Laboratory, for example, said last week that although the revised programme is a "serious fallback" from the original plans, he strongly supports the plan to concentrate on X-ray studies. He pointed out that the HEAO experiment will be much more sensitive than Uhuru, perhaps even picking up several thousand sources compared with about 125 detected by Uhuru. The X-ray detectors on the reconstructed HEAO mission, which will be about 2 square metres, should also be capable of determining individual pulse

shapes from the Crab X-ray pulsar, and perhaps even of picking up the flashes of radiation that some theoreticians have predicted will be discovered coming from the area of black holes.

The new plan has not, of course, pleased everybody. Gamma and cosmic ray scientists are disturbed that if there are cost overruns on the first two missions, the third may be scrapped or at least delayed until the shuttle is available. Their fears may be justified. A year ago, Dr Naugle told the House Committee on Science and Astronautics that the costs of the first two original HEAO missions were then reckoned to be about $180 million, and that even if possible development problems were taken into account, the total cost should be less than $250 million. Last week, however, a NASA press release said that the cost of the original programme would have been about $275 million.

ENERGY

Another Apollo

by our Washington Correspondent

AN energy research and development programme, akin to the Apollo or Manhattan projects, has been proposed by Senator Henry M. Jackson, the Washington Democrat who has effectively staked out the chief claim to energy matters on Capitol Hill. Backed by Senator Jennings Randolf, Chairman of the Senate Public Works Committee, Senator Warren Magnuson, Chairman of the Senate Commerce Committee, and some 25 other senators, Jackson has introduced a bill calling for expenditures of $20,000 million by the federal government on energy research and development over the next ten years. The objective, Jackson said last week, is to make the United States self-sufficient in energy supplies by 1983.

Suggesting that present federal funds for energy research and development programmes are inadequate and illogically distributed, Jackson has proposed that they should be increased to $1,607 million in the 1974 fiscal year, and that they should reach nearly $2,000 million in 1977. This compares with $772 million which the Administration has requested for next year, and which President Nixon proudly proclaimed in his recent message on natural resources.

Jackson's bill also proposes the setting up of an Energy Research Management Project, composed of officials from federal agencies involved with energy matters, to coordinate activities and to fund projects.

The share of the research and development effort devoted to non-

nuclear energy would also be substantially increased by Jackson's bill. It calls for the setting up of five corporations, jointly managed by the federal government and by industry, whose business would be to bring new technologies to the point of commercial application. Specifically, the corporations would be involved with coal gasification, shale oil development, advanced power cycles, geothermal resources and coal liquefaction, and the federal share of the effort would range from 50 per cent in the case of shale oil, to 80 per cent for the development of geothermal energy.

What chance does the bill stand of being passed by Congress? For one thing, it has strong bipartisan support, including the chairmen of the three committees most involved, and for another, as Jackson said last week, it will be considered later this year, when petrol rationing may become a reality in some parts of the United States. "I don't think we will have much trouble getting it passed," he said.

Whether President Nixon will agree to it is, however, another matter. He is now expected to produce his own energy message in late April, but his proposals will certainly be much less extravagant than Jackson's. Congress may have the votes to override a possible Presidential veto, but the Administration would probably not spend all the money even if the bill were rammed through. If the bill is passed in its present form, however, President Nixon would be forced by law to put into effect the institutional arrangements it entails, regardless of whatever he proposes in his own energy message. Jackson has thus neatly scooped the White House.

NEWS AND VIEWS

A New Step in Excitation–Contraction Coupling

IN striated muscle fibres the mechanical response follows the electrical activity of the outer membrane after a very short delay of a few milliseconds. The mechanism connecting the two phenomena has been referred to as excitation–contraction coupling (E–C coupling), an expression coined by Sandow in the early nineteen-fifties. At that time virtually nothing was known about this coupling, except that A. V. Hill had calculated that the diffusion of a hypothetical "activator", liberated by the action potential from the outer membrane, would be much too slow to account for the rapidity of muscle activation.

A great advance towards the understanding of this problem was made when A. F. Huxley and his colleagues provided evidence that the so-called transverse tubules (T tubules: more or less radial invaginations of the outer membrane occurring at every sarcomere) could propagate the excitatory signal to the centre of the fibre. The uncoupling between excitation and contraction produced by the selective disruption of these tubules added further support, and the first step of E–C coupling was thus solved.

The later steps are now also reasonably well understood: the use of intracellular indicators for calcium has clearly demonstrated that in response to the excitation, a massive and sudden increase of Ca^{2+} in the sarcoplasm precedes the onset of the mechanical activity (Jobsis and O'Connor, *Biochem. Biophys. Res. Commun*, **25**, 246; 1966; Ashley and Ridgway (*Nature*, **219**, 1168; 1968). This calcium reacts with the troponin complex located on the thin filaments, relieves the inhibition imposed by this complex on the actin–myosin interaction, and contraction occurs.

But an important question remains to be solved. How does the electrical signal propagated along the T tubules produce this liberation of calcium? This question is particularly fascinating because of the structural relationships between the T tubules (vector of the excitation) and the longitudinal sarcoplasmic reticulum where enormous amounts of calcium are sequestered in the resting fibre. Electron microscopy has revealed that each T tubule is in contact with two lateral dilations of the sarcoplasmic reticulum forming a characteristic "triadic" structure which is repeated once or twice every sarcomere. Obviously the "triadic junction" is a key point of the electrical–calcium coupling.

On page 244 of this issue of *Nature*, Schneider and Chandler report a very interesting observation which seems directly relevant to this question. Using voltage-clamp techniques on muscle fibres, these authors discovered that imposed square pulse depolarizations produce a small outwards current, in conditions where all of the time and voltage-dependent changes in sodium and potassium currents are suppressed (using tetrodotoxin, tetraethylammonium and RbCl). This current decays with time. At the end of the pulse, an inwards current can be detected. The interesting point is that the total amount of charge involved in the "on" and "off" responses is identical and remains so in various experimental conditions.

Schneider and Chandler suggest that the simplest interpretation of this relation is that fixed charges, located in or near a structure sensitive to the polarization, move reversibly in response to changes in polarization. This view is supported by the relation between the amount of charge which moves and the membrane potential. Practically no signal is detected when the holding potential is −100 mV or more negative. For less negative potentials, the amount of charge increases with depolarization following an S-shaped curve, with a mid-point around −50 mV and a maximum value around −20 mV. These figures are illuminating, for the movement of charge occurs in a range of potentials where the mechanical response of the muscle is critically dependent on the membrane polarization. This strongly suggests a connexion with the E–C coupling.

The nature of these charges and their location are unknown. Nevertheless, the speculation presented by the authors at the end of their article is very interesting because they interpret their observation in connexion with the fine structure of the triadic junction. Electron microscope studies of Franzini-Armstrong (*J. Cell. Biol.*, **47**, 488; 1970) have revealed that the mode of contact of the T tubules with the sacroplasmic reticulum is unique among the various types of membrane contacts. The two structures are connected through dense projections ("feet") coming from the terminal cisternae of the sarcoplasmic reticulum, and the space between these feet is in free communication with the sarcoplasm. The density of feet is about 700 per μm^2 of tubule membrane. By comparison, Schneider and Chandler estimate from their results that the density of charge groups is around 300 per μm^2, assuming that they are uniformly distributed on the outer and the T tubule membranes. Though the agreement of these densities might be quite fortuitous, it provides the highly stimulating hypothesis that the excitatory signal is passing from the T tubule to the sarcoplasmic reticulum membrane by way of charges moving in the connecting feet, and Schneider and Chandler have found how to follow the trace of this passage. If true, this is progress.

It remains to be solved how this possible charge transfer across the feet triggers the release of calcium. Schneider and Chandler cautiously suggest that the release is somehow a function of the quantity of charge involved, but the speculation could be pushed a little further. It is probable that the massive and sudden release of calcium produced by the excitation is caused by a permeability change of a large fraction of the sarcoplasmic reticulum membrane (or at least of the terminal cisternae). But the measurements of Franzini-Armstrong have shown that only a few per cent of the sarcoplasmic reticulum membrane are involved in the feet connexion. Therefore, the signal passing through the feet should somehow be "propagated" or "amplified" in order to influence large surfaces of the sarcoplasmic reticulum. In this context, it would be very interesting to see whether a suitable mechanism could be provided by the property of autoamplification of the release of calcium itself, discovered by Ford and Podolsky (*Science*, **167**, 58; 1970) and by Endo (*Nature*, **228**, 34; 1970) and his colleagues.   J.-M. G.

Replacing the Pancreas

THE introduction in 1921 of insulin into therapeutics was a remarkable advance and saved the lives of countless diabetics. Injecting insulin once or twice a day under the skin, however, is by no means the same as the beautifully controlled release of insulin from the beta cell into the pancreatic vein which, together with other homoeostatic mechanisms, severely limits the variation in the levels of blood glucose in the normal individual. Even the best controlled insulin-requiring diabetic experiences swings of blood glucose well beyond the normal. In the fifty years since Banting and Best, improvements in the therapy of the insulin-requiring diabetic have been relatively trivial, though the wide range of insulin preparations currently available, with various properties and formulations, certainly makes it easier to find a treatment to match the individual patient.

Attempts are being made to mimic the natural pancreatic homoeostasis by developing small, implantable glucose sensors which might be connected to an implanted source of exogenous insulin or to some alarm system, warning of excessive hyper- or hypo-glycaemia. J. S. Soeldner has described such a sensor (Diabetes Outlook, 8, 3; 1973) which is about the size of a postage stamp and which, when implanted in the subcutaneous tissue of a rhesus monkey, responds to changing levels of blood glucose. Another sensor has been developed by Bessman and Schultz (Horm. Metab. Res., 4, 413; 1972). These are early days, however, and many technological problems must be overcome before this apparatus becomes an alternative to the pancreatic beta cell. Nevertheless, it is a promising line of research and one in which technology, rather than biology, is the obstacle.

Biology is the major obstacle to another approach—pancreatic transplantation. Experimental heterotopic transplantation has been studied in the dog, but the longest survival has been only 139 days, even with an intensive regime of immunosuppression (Idezuki et al., Surg. Gynec. Obstet., 126, 1002; 1968). In man, most operations have combined kidney and pancreas grafts, the surgery being performed on diabetic patients who had renal failure, in whom prognosis for life was poor. To date twenty-three pancreatic transplants have been reported (J. Amer. Med. Ass., 217, 1520; 1971), the longest survival being one year—better than the dog, but not a very encouraging record. Although the grafts functioned, survival was too short for any adequate assessment of continuing endocrine function by the grafts. But even if the problems of rejection are overcome and results improve dramatically, simple logistics rule out a significant contribution from pancreatic transplantation to the cure, or amelioration, of diabetes.

A possible alternative may be the transplantation of the islets of Langerhans themselves. In recent years a number of techniques have been developed for isolating the islets for various kinds of investigation. In terms of yield, the technique initially described by Moskalewski (Gen. Comp. Endocr., 5, 342; 1965), using collagenase to free the islets from other pancreatic tissues, has proved most useful. A modification of this technique is described by Thomas and his colleagues on page 258 of this issue of Nature. Moskalewski (in The Structure and Meta-

bolism of the Pancreatic Islets, edit. by S. Falkmer, B. Hellman and I. B. Täljedal, Pergamon Press, 1970, p. 73) transplanted guinea-pig islets into various sites in other guinea-pigs and found that they retained the ability to produce and store granules for at least 14 days. Strautz (Diabetologia, 6, 306; 1970) and later Gates et al. (Lancet, ii, 567; 1972) transplanted into genetically-obese mice islets from their lean litter mates. These islets were contained in 'Millipore' diffusion chambers and were implanted intraperitoneally. Not only did the islets survive for at least 10 weeks, but the implanted mice reverted to normal weight and normal levels of glucose tolerance and plasma insulin. Ballinger (Diabetes Outlook, 8, 3; 1973) has reported improvements in the metabolic state of rats made diabetic by streptozotocin injections when islets from normal rats were implanted.

Although many problems remain to be solved before islet transplants can make a significant contribution to the treatment of human diabetes, it seems a more promising line of research than transplantation of the whole pancreas. R. J. J.

Mediterranean Evaporites

THE widespread occurrence of an evaporitic suite in the Mediterranean has been confirmed by the Deep Sea Drilling Project cruise leg 13. The presence of evaporites in the western sea had been suspected from seismic reflexion profiles (Hersey, Bull. Geol. Soc. Amer., 76, 1251; 1965) but their age remained debatable until the drilling proved that they are Upper Miocene. The evidence from leg 13 creates more controversy, however, in this case about the environment and mode of their formation.

Three possible models could account for the origin of the evaporites. In the first, a deep basin, renewed by water from the Atlantic, maintains its level during evaporation at the world-wide sea level; this is the "deep water, deep basin model". In the "shallow water, shallow basin model", connexion with the Atlantic permits the brine level of a shallow basin to remain at world-wide sea level. A third "desiccated deep-sea basin model" allows the evaporation of a series of salt lakes or playas, which lay several thousand metres below the sea level of the Atlantic.

The evaporitic suite obtained from drilling during leg 13 comprises halite, anhydrite, gypsum and dolomite. All available evidence from mineralogical, petrographical, sedimentological and geochemical investigations indicates that these evaporites were in fact formed in shallow water. The presence of anhydrite in nodular and "chicken-wire" form strongly suggests a subaerial environment of origin, similar to present day Sabkhas of the Persian Gulf.

Cyclic deposits, discovered in a hole to the south of Mallorca, reveal sequences, suggestive of deeper to shallow-water formation, which consist of laminated dolomites through to stromatolites; these indicate that periods of inundation successively follow periods of desiccation. The scarce fauna and flora contained in the carbonate sediments are of brackish water association, whereas the halite beds are barren. The latter also show signs of desiccation and replacement by anhydrite crystals, possibly during subaerial erosion. It is apparent also from marine inter-

calations within the evaporites that intermittent flooding of a desiccated basin has occurred.

A further indicator of a shallow water environment is the distribution pattern of the evaporites. Typically, playa deposition constitutes a "bull's eye" zonation of concentric zones of salts, with the inner zone the most soluble, that is halite in this series. This seems to be the case, for halite coincides with the areas of deepest water in the western basin, whereas it was not found in the east. A restricted basinal type of deposition would require a "tear drop" pattern of deposition, where less soluble salts occur near the opening and soluble salts at the far end. With the limited coverage attained by JOIDES sites, however, it is difficult to speak authoritatively on this matter.

The greatest disagreement emerges during discussion of the depth of the basin itself, the salient problem being whether the water level altered intermittently or whether the bottom of the basin moved up and down catastrophically to produce the great thicknesses of evaporites attained in the Mediterranean. Hsü *et al.* (*DSDP Initial Reports*, II, 43, 1203 ; 1973 ; and page 240 of this issue of *Nature*) favour the existence of a deep depositional basin largely on the strength of palaeontological evidence. The sediments immediately overlying the evaporites contain deep-water foraminifera of Pliocene age, whose appearance would be difficult to envisage in the event of an inundation of a shallow basin of Upper Miocene age. Also the sediments of Middle Miocene age cored from the Hellenic Trench are of deep water pelagics so that it seems probable that the basin had a generally deep base level. Geomorphological evidence has been recognized by Hsü *et al.* from adjacent land areas, where channels, cut by streams rejuvenated during regression of the sea, have been infilled by alluvial and terrestrial clastics. Steeply graded canyons are apparent at the continental margins, and these are probably drowned river valleys of Upper Miocene age. Nesteroff (*DSDP Initial Reports*, II, 21, 673 ; 1973), however, describes these canyons as a rejuvenated Middle Miocene system which was recut during subaerial erosion in a shallow basin. This is one example of a series of data which may be adapted to fit either hypothesis.

Finally, Nesteroff uses the evidence of local vertical tectonic activity of post-Miocene age in the Mediterranean area to argue for a shallow basin formation. His model requires the existence in the Serravallian of several shallow basins, of restricted circulation and connexion, which became completely cut off from the Atlantic during the Messinian. Desiccation followed, and was relieved only by periodic influxes from the Straits of Gibraltar. These permitted the accumulation of great thicknesses of evaporites in a central trough and thinner peripheral deposits on the slopes of the basins. Then, during the Pliocene transgression, deep pelagic oozes were deposited and vertical movements led to the subsidence of the basins and uplift of the surrounding margins.

On the other hand, there is Hsü's picture of a deep hole, intermittently refilled during the Messinian by overflow from the Straits of Gibraltar, the brine content in the basins being successively replenished. The progress is recorded by the interbedded marine marls of the Upper Miocene evaporite formation of Sicily. The facts are inadequate to prove either hypothesis fully ; neither will be credible until further drilling reveals the detailed sequence of pre-evaporite sediments.

From a Correspondent

Unique Sequences in Eukaryotic mRNA

IN next Wednesday's *Nature New Biology* (March 28) Dina, Crippa and Beccari describe experiments designed to determine whether or not there are, in a population of mRNAs from developing *Xenopus* embryos, sequences transcribed from reiterated DNA.

Labelled polysomal mRNA extracted from dissociated *Xenopus* embryos was found to have a high specific activity and was shown to be free from contamination by labelled ribosomal sequences. These features, combined with the use of stringent hybridization conditions to prevent degradation of RNA during the annealing reaction, provided the basic requirements for successful RNA hybridization with DNA in excess.

When *Xenopus* mRNA was annealed to DNA, only 5 per cent of the input RNA hybridized before a $C_o t$ of 10^{-1}. At $C_o t$ 100, 13 per cent had hybridized and the rest of the hybridization followed kinetics similar to those of unique sequences reaching a final value of 61 per cent between $C_o t$ 5×10^3 and 2×10^4. In ideal conditions for DNA excess hybridization, however, up to 90 per cent of input RNA should be hybridized.

Using a filter trapping method mRNA reassociated with DNA starting with a very low $C_o t$ 10^{-2} and at $C_o t$ 100 the reaction was complete when 80 per cent of the input RNA was retained by filters. The hybridization curve revealed two main components renaturing at different rates with $C_o t$ 1/2 of 5×10^{-2} and $C_o t$ 1/2 20 to 30. Only a small percentage of the RNA bound to filters, however, was RNase resistant.

The melting profiles of DNA/mRNA hybrids obtained at low (100) and high (3,000) $C_o t$ values are practically identical ; they are very sharp and have T_ms very close to the T_m of native *Xenopus* DNA. These facts suggest that the hybrids which are formed are very specific, and, because they are so similar to the melting curve of DNA, there must be some mRNA complementary to rapidly renaturing reiterated sequences.

Dina *et al.* suggest that these results are best explained if one supposes that each mRNA molecule consists of a part which hybridizes to repeated sequences and a second part which is complementary to a unique sequence. Thus, in the filter trapping experiment, the repetitive part of the mRNA molecule hybridizes rapidly to reiterated DNA ; the rest of the molecule is also retained by the filter and complete (80 per cent) retention is obtained at a low $C_o t$ 100. They also suggest that the long incubation times required for high $C_o t$ values lead to thermal breakage of the partially hybridized mRNA. The RNA fragments broken off would contain unique sequences which would then hybridize more slowly, giving rise to the 61 per cent hybrid obtained at the end of the annealing reaction.

If each mRNA molecule consists of a fast and a slow annealing part then partial degradation of the mRNA molecules should shift the kinetics of reannealing. When alkaline digested mRNA was hybridized to DNA the kinetics were similar to the reaction with intact mRNA up to a $C_o t$ 50. But in this case hybrid formation reached a final value of 90 per cent of input RNA at a $C_o t$ of 2×10^4.

These results indicate that each mRNA molecule contains a main part, which is transcribed from unique DNA, and a covalently linked small part transcribed from a family of homogeneously repeated sequences. If repeated sequences are bound to many different unique sequences they should be found dispersed throughout the genome. Indeed when DNA was fractionated on $CsCl_2$ the mRNAs hybridized to main band DNA and not to satellite DNA.

RABIES

Problems of Control

from our Medical Virology Correspondent

RABIES is not declining ; on the contrary it is spreading throughout the world especially among wild animals. Rabies virus is classified as a member of the rhabdovirus group, which contains a diverse collection of bullet-shaped RNA viruses including vesicular stomatitis virus with a bovine host, Egtved virus of rainbow trout, Marburg virus (see *Nature*, **233**, 236 ; 1971), Sigma virus of *Drosophila*, Flanders-Hart Park virus with a mosquito host, potato yellow dwarf virus, maize mosaic virus and others.

Rabies virus is transmitted by contact, usually through a bite ; there are no known vectors. It spreads from the site of infection along the peripheral nerves towards the central nervous system through nerve-associated tissue spaces, although this is by no means certain. Similarly, there is no explanation for the dysfunction caused by the virus in the central nervous system because only minimal cytocidal effects are usually observed in cells infected with rabies, but the host's immune response may contribute to the pathological effect.

Rabies is enzootic in all the continents except Australia and Antarctica. Many of the large islands, however, such as Britain, Cyprus, Hawaii and New Zealand are free of the disease largely because of rigidly enforced quarantine regulations concerning the entry of dogs, cats and other animals. From the standpoint of human infection, the dog has remained since ancient times the most important reservoir and transmitter of rabies. Wildlife rabies, on the other hand, constitutes the greatest problem in many areas; knowledge of the ecology of wildlife rabies, however, is fragmentary.

In Asia the pariah dog is the principal carrier of the disease, although jackals are frequently involved. Mongooses and meerkats are important rabies reservoirs in South Africa and vampire bats in Central and South America. In the United States the skunk is the most important transmitter in certain areas and bats in other regions. Sledge dogs and silver foxes are mostly affected in the Arctic region. Badgers often live in close propinquity to foxes and have been frequently infected in the current epizootic of fox rabies in central Europe (M. H. Kaplan, *Nature*, **221**, 421 ; 1969).

The present epizootic of fox rabies in Europe is particularly disquieting. The problem is best illustrated by the following incidents. At the end of last December a 20-year-old American soldier reported to a hospital in Saigon with clinical signs suggestive of rabies. He died two weeks later. This man had played with a stray puppy on November 14 and was slightly bitten on the hand. Another serviceman also bitten by the same dog reported the incident. The dog was confined and died 3 days later of rabies. The second soldier, however, was treated successfully (Communicable Disease Centre, *Zoonosis Surveillance*, February 1973). In another US Air Force base in Vietnam a puppy was adopted in the officers' quarters to be registered as a mascot. The puppy was involved in a fight, was scratched on the face and ultimately developed rabies. Thirty-one persons, in the meantime, were possibly exposed to infection at a party held in the officers' quarters and rabies prophylaxis, unpleasant at the best of times involving up to twenty-one inoculations and not infrequently with serious side-effects, was instituted for twenty-three persons (R. Moser, *Aerospace Medicine*, **43**, 778 ; 1972). These two incidents bear an important message for Britain because the principal risk of introduction of rabies to the country is by the irresponsible smuggling of dogs and cats ; with the belt of rabies advancing in Western Europe this is a real hazard.

Human rabies prophylaxis is based chiefly on two types of vaccine (S. A. Plotkin and H. F. Clark, *J. Infec. Dis.*, **123**, 227 ; 1971). The efficacy of the nervous tissue vaccines, Semple and Fermi, has not been evaluated by controlled studies. The duck embryo vaccine has been favoured because of the lower risk of allergic encephalitis, although better antibody responses are invoked by the Semple vaccine. There are also several experimental vaccines. The Flury-HEP vaccine is a live virus passaged 180 times in chick embryos, but it elicits a poor antibody response and it is not suitable for use after exposure. Semple-type vaccines using suckling mouse brain are available in some countries. More promising are rabies vaccines prepared in tissue cultures which completely lack nervous tissue and, therefore, are not expected to be encephalogenic. The outlook for man is thus hopeful and indeed currently between 700,000 to 1,000,000 persons are subjected annually to a rabies immunization regime ; but the problem of controlling wildlife rabies remains an impossible task.

NEUROPHARMACOLOGY

Opiate Receptor Binding

from a Correspondent

WITH federal support of basic research plummeting, bioscientists in the United States are hastily reviewing their research for evidence of social significance. One group that will not have far to look is Snyder's team at Johns Hopkins University Medical School. In a recent issue of *Science* (**179**, 1011 ; 1973) Pert and Snyder announce their identification in mammalian nervous tissue of a receptor which specifically binds opiates.

Binding was demonstrated by incubating tissue homogenates with tritium-labelled naloxone, a potent antagonist which precipitates withdrawal in humans addicted to opiates. Naloxone, rather than an agonist such as morphine, was chosen on the premise that as an antagonist its binding would be less reversible, and thus the drug-receptor complex might hang together long enough to be measured. After incubation, the homogenates were washed through a filter which trapped large

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Lepore and Anti-Lepore Haemoglobins

THE "Lepore" and "anti-Lepore" haemoglobins are of great theoretical interest because they illustrate at a molecular level the consequences of the process of gene crossing-over. The non-α chain of Hb Lepore-Hollandia, the first example of this type of haemoglobin variant to be discovered, was found to contain N-terminal and C-terminal regions derived from normal δ and β chains respectively. In 1964 Smithies showed how such a chain could arise from homologous but unequal crossing-over of the δ and β chain genes. Haemoglobins Lepore-Boston and Lepore-Baltimore differ in the relative lengths of the δ and β segments of the δ-β chain.

In *Nature New Biology* next Wednesday (March 28) Badr, Lorkin and Lehmann now report that the non-α chain of Hb P-Nilotic is a reversed or anti-Lepore β-δ chain, with the N-terminal region derived from the β chain and the cross-over occurring between positions 22 and 50. This clearly distinguishes it from Hb P-Galveston (β-117, G19, His$\rightarrow$Arg) which has the same electrophoretic mobility.

Purified Hb P-Nilotic has a slightly higher oxygen affinity than Hb-A, but the haem-haem interaction and Bohr effect are very nearly identical. It is the second anti-Lepore haemoglobin to be described. The other is Hb-Miyada, in which the β-δ cross-over occurs before position 22, so that its electrophoretic mobility is the same as that of Hb-A$_2$.

As Lehmann and his colleagues point out, it will be of great interest to study the biosynthesis of the β-δ chains of Hb P-Nilotic to ascertain if this occurs only in the earlier stages of erythroid cell maturation, as is the case for the δ chain of Hb-A$_2$ and the δ-β chain of Hb-Lepore.

molecules such as receptors but let through the smaller, unbound naloxone molecules. The filters were then counted to determine the amount of radioactivity bound to them.

It was necessary to demonstrate that the tritiated naloxone trapped on the filters was specifically bound to receptor molecules and not just stuck unspecifically to macromolecules. This was achieved by adding opiate agonists such as levorphanol, morphine, or methadone to the incubation mixture. The analgesic effect of opiates *in vivo* is very stereospecific; activity is almost completely limited to isomers orientated analogously to D(dextro-rotary)-morphine. Thus, if the physiological response parallels receptor affinity, D isomers of the opiates should bind much more readily than their L isomers. This was found to be the case: low concentrations of D-isomer opiates drastically reduced naloxone binding (by competing for the receptor sites), whereas the L-isomers were without effect. In this fashion 75 per cent of the radioactive naloxone trapped on the filters was determined to be bound stereospecifically. Furthermore, the affinities of the various opiates for the receptor corresponded to their relative potencies for producing analgesia.

Further evidence for specificity of binding was seen by the fact that specific binding was maximal at physiological temperature (37° C) and almost nonexistent at 4° C. Specific binding was also pH dependent, peaking at pH 7.4.

In this investigation opiate receptor binding was found exclusively in neural tissue. Several investigators have used contraction of the guinea-pig small intestine as a physiological indicator of response to opiates. Pert and Snyder demonstrate that de-innervation of the intestine completely abolishes specific binding.

What is the function of the opiate receptor? It hardly seems likely that vertebrate nervous systems possess a sensitive receptor for a molecule that is not normally found in vertebrates. More likely, the opiates are acting as analogues of some endogenous molecule. Whatever the nature of this molecule, it is undoubtedly important and its elucidation may significantly advance understanding of neural function.

Even before the theoretical implications of the opiate receptor are worked out, this technique is likely to attract widespread attention. As Pert and Snyder laconically point out, their assay offers a simple means of rapidly scanning the relative effects of potential narcotic agonists and antagonists. This could prove a valuable tool for bioscientists bent on finding a medical solution to the problem of drug abuse.

TRANSFER RNA
Clues on Conformations

from our Molecular Biology Correspondent

TRANSFER RNA needs magnesium to maintain its functional conformation, in a specific manner that is not to be equated with the mere stabilization of base pairing by increasing ionic strength. This observation led to the recognition of a relatively well-defined "denatured" state, with apparently marginally less base pairing than the native, but differing from it by a wide selection of criteria. Whether the denatured state of transfer RNA has any functional role in the cell is questionable, but it is of interest particularly for what it might tell one about the way in which the chain selects one among many possible alternative base-pairing schemes in a given set of conditions. The conformation of one, and as the crystallographers would undoubtedly maintain, the native form of a tRNA should be explicitly known soon, and has already been adumbrated. It is not, however, clear that other conformational isomers can be crystallized, and recourse to indirect methods of evaluating the secondary structure, or at least how it differs from that of the native molecule, is therefore inescapable. So far the most convincing attempts at defining these differences have originated from experiments on the binding of oligonucleotides to available unpaired parts of the chain, and from examination of the sites of scission by nucleases.

A curious variation on this last approach has been evolved by Wintermayer and Zachau (*Biochem. Biophys. Acta,* **299,** 82; 1973) who have discovered an unsuspected specificity in metal-catalysed alkaline hydrolysis. With magnesium as catalyst, chain scission ensues at pH 9.5 and 50° C, and fragments progressively appear in electrophoretic gels. With yeast phenylalanine-tRNA, if the magnesium : phosphate ratio is greater than about 0.5, two fragments are formed with a high degree of

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The Identity of Cytotoxic Cells

THE revolution in cellular immunology which led to the concept of two principal classes of lymphocytes, T cells of thymic origin and B cells originating from the bone marrow or a bursal equivalent, has passed its phase of turbulence. Emphasis is now changing, on the one hand, to clarification of the various descriptive characteristics of the two classes of cell and, on the other hand, to elucidation of their functional capabilities. Clearly in the long run these two avenues of approach should be confluent; at present they are not.

It has been argued in relation to anti-tumour immunity that T cells can be cytotoxic against malignant cells but that their aggressive effect may be inhibited by antibody which is a B-cell product. B cells, on the other hand, have apparently been shown to be cytotoxic but their killing potential requires an antibody-sensitized target cell. The complicating feature of the whole response pattern is that the production of both blocking and sensitizing antibody (possibly the same entities) may well require cooperation between T and B cells. In next Wednesday's *Nature New Biology* (March 28) Greenberg *et al.* suggest that B cell cytotoxicity is brought about by a class of B cell lacking detectable surface immunoglobulin.

Greenberg *et al.* investigated the capacity of normal (Balb/c) mouse spleen cells to lyse chicken erythrocytes *in vitro*. The target cells were previously sensitized by incubation in a rabbit anti-chicken erythrocyte antiserum. After depleting the spleen cells of macrophages by incubation with iron carbonyl and of immunoglobulin-bearing (B) lymphocytes by passage through a 'Sephadex' column which had been coated with a heterologous anti-mouse Fab, the cytotoxic potential of the remaining cells was found to be greater than that of the starting cell population. Furthermore, when the B cells were released from the 'Sephadex' column by incubation with dextranase they exhibited no cytotoxicity.

Greenberg *et al.* then took the cell effluent from one of their anti-Fab coated columns (without dextranase treatment) and reacted it with a heterologous anti-T cell antibody in the presence of complement. This device reduced the number of viable cells by 82 per cent, presumably by killing the T cells present, but failed to alter the cytotoxicity against sensitized chicken erythrocytes. Along similar lines it was shown that the spleen cells of mice depleted of T cells by a schedule of neonatal thymectomy, irradiation and treatment with an anti-lymphocytic antiserum were usually cytotoxic in the test system.

The authors conclude from these experiments that there exist cells which are not T cells and which do not have immunoglobulin on their surfaces (a usually accepted characteristic of B cells) but which nevertheless can be cytotoxic against sensitized nucleated cells. They indicate the possibility that such cells are not lymphocytes. Thus the nice neat division of cytotoxic lymphocytes into T and B depending on whether they are blocked or potentiated by antibody may not necessarily be true.

specificity. From the size of these fragments, and the presence of dihydrouridine in both, it follows that the primary site of scission is between positions 16 and 17, that is to say, in the dihydrouridine loop. This remains true when the bulky Y base is first chemically excised from its position in the anticodon loop, and seems to extend equally to serine-tRNA. If the magnesium concentration is reduced below the critical value, catalysic efficiency is unimpaired, but a striking change occurs in the fragmentation pattern, with advent of new components, in particular a large piece of nearly seventy nucleotides. There is circumstantial evidence to identify this as residues 11–76.

If the conformation is further and more drastically weakened, by addition of 7 M urea, the hydrolysis becomes totally non-specific. The inference from these results is that the alkaline hydrolysis proceeds by way of a cyclic phosphate intermediate, which can only form when there is sufficient local chain flexibility. This condition is presumably fulfilled at the bond joining the non-aromatic nucleotides (which do not stack). The absence of hydrolysis at other sites in the chain points to a rigid structure, which is noteworthy particularly as regards the anticodon loop. At lower magnesium concentration at the working temperature, a transition to a state with more degrees of conformational freedom evidently occurs, and this is very likely a still highly base-paired denatured form.

The conformational difference between the native and denatured states is quantitatively reflected in the tritium-exchange experiments of Webb and Fresco (*J. Mol. Biol.*, **74**, 387; 1973). The kinetic profiles are strikingly different in the two forms, with much faster exchange in the denatured. This again is not simply an electrolyte effect, for with a leucine-tRNA, which has the property found in some but not all species, of a high activation barrier between the two conformations, so that it can be trapped in either at will in the same condition, the kinetic difference persists in its entirety. Evaluation of the total number of slowly exchanging hydrogens leads to a value of 111 for native leucine-tRNA and 95 for denatured. This indicates that a few more bases are paired in the native state, though the precise allocation of numbers of exchangeable protons to A·U and G·C base pairs (let alone any G·U pairs that may exist) involves a margin of uncertainty. The differences in exchange rates are thought to be related to tertiary structure, which is certainly more compact in the native molecule.

Webb and Fresco offer a further observation, which may bear on the mechanism of the conformational transition. This has a high activation energy (of the order of 70 kcal mol⁻¹ for renaturation), which suggests that to permit the structural rearrangement momentary opening of one or more base-paired tracts must occur. If such a transitional state were to persist for a sufficient interval of time, it should manifest itself in a sudden release of exchangeable protons, and this is exactly what Webb and Fresco report. Introduction of magnesium into unfractionated tRNA at an early stage of exchange causes the kinetics to lurch abruptly onto a new smooth curve. Webb and Fresco are properly cautious, for the suggested interpretation would have the unpleasing implication that the barrier is actually diminished by magnesium, which would normally be expected to stabilize all base-paired states relative to the unfolded. Moreover, such a very long-lived intermediate should manifest itself in the relaxation kinetics of the transition, and this has not been observed.

That a significant difference in the extent of base pairing actually exists, as between the native and denatured leucine tRNA, is shown by Wong *et al.* (*ibid.*, 403), using high-resolution proton magnetic resonance spectroscopy in water solution, where downfield resonances arising from slowly exchanging protons involved in base pairing can be resolved. With the aid of assignments based on earlier work, three to five G·C pairs are shown to be lost on denaturation, and up to two A·U pairs possibly gained. Wong *et al.* note that in the leucine-tRNA the dihydrouracil

stem comprises only three G·C pairs, and is thus an obvious candidate for the site of the conformational difference. This would be consistent with the greater accessibility of this region to complementary oligonucleotides in the denatured molecule.

TRANSCRIPTION

New Termination Factor

from our Cell Biology Correspondent

A SMATTERING of Greek, or at least knowledge of the Greek alphabet, seems to be an essential requirement for anybody wishing to matriculate in the study of transcription by bacterial DNA-dependent RNA polymerase. Following the Hellenic inclinations of Travers and his associates, and Roberts, who selected sigma and rho to designate the factors which they discovered, Schäfer and Zillig have named as kappa a new termination factor, which blocks the transcription of phage T4, T5 and T7 DNA by *Escherichia coli* RNA polymerase (*Europ. J. Biochem.*, **33**, 201; 1973).

This new termination factor, kappa, was discovered when Schäfer and Zillig set out to isolate rho factor and is apparently a dimeric protein made of two identical subunits, each with a molecular weight of 17,000. It is present in *E. coli* cells at a concentration about the same as that of RNA polymerase; that is to say, each cell probably contains several thousand molecules of kappa. Kappa binds to DNA and does not inhibit initiation of tran-

Screen for Human Tumour Viruses

MURINE sarcoma virus (MSV) is defective; the virus transforms susceptible fibroblasts, but it cannot replicate infectious progeny in the cells that it transforms unless they are coinfected by a murine or other mammalian leukaemia virus which complements the defect of the MSV genome.

Mouse cells transformed by MSV in the absence of a leukaemia virus helper are described as S⁺L⁻, and such cells can be used to test whether or not a stock of any virus contains helper activity for MSV because if the virus has such helper activity it should infect S⁺L⁻ cells and cause the release of infectious MSV. As Peebles, Fischinger, Bassin and Papageorge report in *Nature New Biology* next Wednesday (March 28), human amnionic cells can be transformed by certain strains of MSV to yield human S⁺L⁻ cells which should prove useful in the identification of putative human leukaemia viruses.

To induce MSV to transform cloned human amnionic cells Peebles *et al.* rescued MSV from mouse S⁺L⁻ cells

by superinfection with feline leukaemia virus. The rescued virus is a pseudotype, it has the MSV genome in a feline leukaemia virus envelope and is designated MSV(FeLV). This pseudotype virus, because it has a feline leukaemia virus envelope, can infect human cells and, as Peebles *et al.* found when human amnionic cells are infected with MSV (FeLV), clones of transformed human S⁺L⁻ cells can be isolated.

These human S⁺L⁻ cells do not release infectious sarcoma viruses, but if they are superinfected with feline leukaemia virus they begin to release MSV(FeLV) pseudotypes and if they are superinfected with RD114 virus, a candidate human C-type RNA tumour virus, they release a pseudotype MSV (RD114). Together with untransformed human amnionic cells, these human S⁺L⁻ cells may, therefore, as Peebles *et al.* conclude, "provide a unique *in vitro* method in a human system for the isolation, assay and identification of sarcomogenic and leukaemogenic RNA tumour viruses from human tumours".

scription, although it does reduce both the rate and the extent of transcription. In the presence of saturating amounts of kappa the average length of phage RNA transcripts is about 40–50 per cent that of transcripts made in its absence. Analysis by sucrose gradient centrifugation and by competition and saturation hybridization indicates that only a few of the kappa molecules bound to phage DNA halt transcription, and most of the bound kappa seems only to reduce the rate of transcription. Once transcription is halted by a kappa molecule bound at low ionic strength to specific kappa termination sites, the RNA transcript, the DNA template, the kappa molecule and polymerase remain associated in some quaternary complex and, according to Schäfer and Zillig (*ibid.*, 215), this is also the case when transcription is terminated by factor rho.

Having isolated kappa, Schäfer, Zillig and their associates (*ibid.*, 207 and 215) investigated the influence of factors and ions on the initiation as well as the termination of transcription by *E. coli* RNA polymerase. Their data on the rate and pattern of initiation of transcription of native T4, T5 and T7 DNA by RNA polymerase containing sigma factor, in conditions of low and high ionic strength, and in the presence and absence of heparin, led them to an interesting model of a possible sequence of events leading to initiation. Schäfer *et al.* propose that the promoter site on DNA is functionally differentiated into an entry site, R, to which the RNA polymerase molecules bind. They further postulate that the enzyme molecules are then shunted to a storage site, S, where they can become stably aligned and associated with a template before moving to the actual initiator site, I. Whether or not this model of a differentiated promoter can be verified remains to be seen.

And what about termination? Transcription of T7 and T5 DNA in the absence of factors is terminated in conditions of both high and low ionic strengths with the release of RNA, but polymerase is only released at high ionic strength. With T4 DNA as template and at lower ionic strength neither the enzyme nor the RNA transcript is released. At low ionic strength, in the presence of termination factors rho and kappa, transcription of T4, T7 and T5 DNAs is terminated without the release of enzyme or RNA transcript. Just how rho and kappa act *in vivo* and how they are counteracted has yet to be elucidated.

In the same issue of the *European Journal of Biochemistry* (*ibid.*, 301) Smith reports experiments probing another initiation event — the initiation and translation of EMC virus RNA in a cell free system from Krebs II ascites cells. This work not only supports the

argument that met-tRNA$_f^{met}$ is the universal initiator of translation in eukaryotes, but also that the EMC RNA, which codes the nine proteins at least *in vivo*, has a single initiation site for translation and that the polypeptide made immediately after the initiation site is metabolically labile and not part of any of the nine EMC proteins.

SELENOLOGY

Moon Matters

from a Correspondent

THE First Lunar Science Conference in January 1970 was almost entirely devoted to reports of lunar sample investigations. Subsequent conferences have, however, broadened in context and the most recent conference, held from March 5 to 8 at the Johnson Space Center, has included accounts by both Apollo 16 and 17 astronauts, theoretical contributions both on the formation of the mascons and the origin of the Moon, Soviet analyses of material from Luna 16 and 20, and descriptions of experiments carried out on the lunar surface and from lunar orbiting spacecraft. It is also apparent that there is a big increase in the number of experiments aimed at laboratory simulation of lunar conditions and processes.

Many new interesting results concerning the immediate lunar surface layer were reported. An infrared radiometer (Professor F. J. Low, Rice University, and Dr W. W. Mendell, NASA) was used to scan the lunar surface from the Apollo 17 service module. The results show night-time surface temperatures below 90 K, indicating a considerably lower surface thermal conductivity than had been previously assumed. Dr H. Mizutani (Caltech, Pasadena) reported that the insulation of this layer may have appreciable effect on the thermal evolution of the Moon. Dr A. Dollfus (Meudon Observatory, Paris) described the extension of his work on optical lunar polarimetry which now reveals widely differing properties of the surfaces of the asteroids. The carbon in the lunar surface layer now seems to be entirely the result of absorption of that element from the solar wind. Dr G. Eglinton (University of Bristol) and others gave evidence to show that this carbon is converted to iron carbide during the melting process associated with meteoritic bombardment and is later distributed throughout the broken regolith layer by subsequent meteoritic churning of the surface. Mineralogical arguments were put forward to show that the glass globules found in the regolith have cooled at rapid rates ($\sim$ 100 K

Red Palaeosols Found in Northern England

RED palaeosol features found in sandstones and shales in the north of England provide a clue to the climate of the area in Pleistocene times. In next Monday's *Nature Physical Science* (March 26) Bullock, Carroll and Jarvis describe three such palaeosols which they have found, and a fourth reported by Curtis. All four are in Yorkshire (see map); red mottles occur in clays 13 km northwest of Scarborough, sandstone blocks with a red rind are found in the Langdale Forest 16 km north-east of Pickering, brown and yellowish-brown sandy clay loam and occasional red mottles 10 km west of Scarborough, and a "white material with many ferruginous concretions" below a thin iron pan 10 km north of Pickering.

What is the significance of these features? According to Bullock and his colleagues, they are all similar to features commonly reported in regions of the tropics and sub-tropics which have marked wet and dry seasons. In Northern Nigeria, for example, all four kinds are found in a single landscape, as seems to be the case in Yorkshire. It seems reasonable to conclude that during the Pleistocene, when these deposits were formed, the climate of the region —and presumably of the rest of Britain —was of that kind. But the red mottles in shale and red rinds and clayey

weathering in sandstone only seem to be present in a 50 (km)^2 area, although the rock types are common in England.

It may be, argue Bullock *et al.*, that widespread glaciation has denuded large areas, removing similar features in other parts of the country. This could explain why these particular palaeosols are now found only on plateaux, protected by escarpments and sea cliffs. This immediately suggests suitable regions where similar features can be expected, and Bullock *et al.* point specifically to small plateaux at the edge of the Pennines as strong candidates, north and east of the presently known sites.
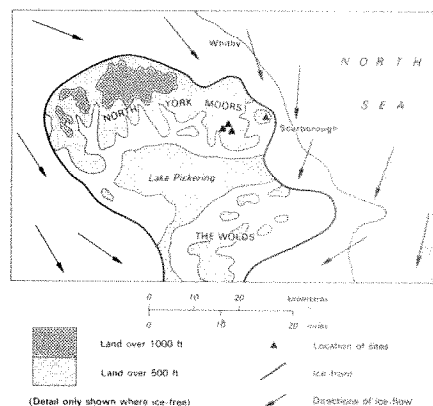
Red palaeosol sites and patterns of ice movement in the late Devonian, in East Yorkshire.
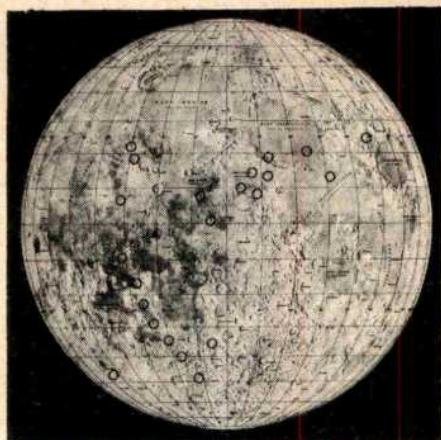
The near side of the Moon showing the epicentres of moonquakes recorded by lunar-based seismometers.

s^{-1}) in free flight above the lunar surface (Dr W. von Engelhardt, University of Tübingen). The orange soil near the Apollo 17 site was shown to consist chiefly of coloured glass. The most striking region, located in a cylinder 1 m in diameter and 0.3 m deep, showed no evidence of recent volcanic activity, but was formed nearly 4×10^9 yr ago and has been exposed near the surface for about 3×10^7 yr.

The installation of a network of lunar-based seismometers has led to some of the most impressive results of the whole Apollo programme. The outer 20 to 30 km of the Moon has been shown to be broken or fractured so that the propagation of seismic energy within this layer may be regarded as a diffusion process. The seismometers have also detected the impact of many large meteorites on the lunar surface, measuring both the energy and position of the impact. The statistics of such observations are in good agreement with other (often less reliable) estimates of meteorite flux.

Internal centres of lunar seismic activity have been located principally between 800 and 1,100 km below the surface (lunar radius 1,738 km). At the conference Dr G. Latham (University of Texas, Galveston) reported that the epicentres for such events (moonquakes) lie close to two great circles (see Figure). He also discussed the impact of a large meteorite near the Sea of Moscow on the lunar far side. The shear waves from this impact were completely suppressed by the central zone of the lunar interior and this may imply central temperatures as high as 1,800 K—a value many hundreds of degrees above that inferred earlier from observations of the response of the Moon to the electromagnetic field associated with the solar wind.

The sites chosen for the Apollo landings have moved progressively from the flat dark marial regions to lighter more rugged upland areas. The last two landings, in particular, have investigated regions with kilometre scale mountains, large boulders many metres in size and even outcrops of rock. Subsequent terrestrial analysis of these rocks has shown that very few of the samples are similar to the Apollo 11 and 12 basalts, formed in the maria by solidification of large volumes of magma or lava. Instead these upland rocks are breccias, that is composite rocks formed by the compaction of powdered or broken rock under the influence of temperature or pressure. Breccias were also returned from the maria but the upland breccias are composed of particles of comparatively primitive anorthitic rock. These breccias range from fragile low-density samples to dense rocks which have undergone heat treatment in the lunar surface layer at temperatures well above 1,000 K and in some cases almost sufficient to return them to molten magma. This history has been confirmed by magnetic measurements reported at the meeting which indicate cooling from temperatures above the Curie point in the presence of magnetic fields estimated in the range 10^{-4} to 10^{-6} tesla (1 to 10^{-2} oersted). Still higher fields are required by magnetometer measurements carried out on the lunar surface. A dynamo mechanism in a once liquid lunar core could possibly produce such a field, but a more attractive possibility may be an early intense solar field invoked in modern condensation and accretion models for the origin of the Solar System.

Whatever the origin of this early magnetic field its discussion at this conference has demonstrated clearly that lunar science is not simply an isolated study. The antiquity of the lunar surface on a cosmological time scale makes it ideal for experiments concerning changes in the rate of solar flare activity, the flux of meteorites and the cosmic-ray flux. Rarely regarded as intellectually respectable, erratically if lavishly supported by a few countries, lunar science has now returned to the stage where its adherents are chiefly motivated by scientific interest.

GLOMAR CHALLENGER

Red Sea Drilling

from our Geomagnetism Correspondent

IN view of the importance of the Red Sea as a region of apparently young seafloor spreading, the results of the visit to the area last year by the deep-sea drilling vessel Glomar Challenger are awaited with some anticipation. Full details will presumably become available slowly over the coming months and years ; but in the meantime Ross et al. (Science, **179**, 377 ; 1973) have reported preliminary results and conclusions derived on board during the voyage.

Three of the six holes drilled (225 to 230) were in the vicinity of the well-known hot brine area comprising the Atlantis II, Chain and Discovery Deeps where waters of high salinity and temperature are underlain by sediments enriched in heavy metals such as copper, lead, zinc, silver and gold. The core from site 225, which lies 16 km east of the Atlantis II Deep, indicated 177 m of late Miocene to late Pleistocene silt and ooze overlying 53 m of anhydrite and halite. The surface of these evaporites was found to correlate with the acoustic reflector S (velocity 4.4 km s^{-1}

Amino-acids in Lunar Samples

IN next Monday's Nature Physical Science (March 26) Modzeleski et al. report their analyses of seven samples brought back from the Moon by the Apollo 14 astronauts for carbon compounds and amino-acids. They used a combined vacuum pyrolysis-mass spectrometry technique for estimating gases containing carbon and hydrocarbons and ion exchange chromatography for quantifying the amino-acids. These latest results are part of an ongoing attempt to elucidate the history and manner of formation of these molecules on the Moon.

The principal gaseous products of the pyrolysis procedure were CO, CO_2 and CH_4, and the results of pyrolysing 50 mg portions of the lunar samples indicated that carbon was present in the gases to the extent of between 76 and 161 parts per million. The largest relative amount of CO and CO_2 was given off by a breccia sample rather than by a sample of fines.

When the mass spectrometer was set to record compounds with a larger molecular weight, many species came to light, for example C_2H_5, C_3H_5 and COS. And sulphur was clearly evident as a ring above the cold trap of the pyrolysis tube. Modzeleski et al. say that their findings suggest that the sulphur was not present in elemental form nor in an organic compound but probably in a mineral in view of the high temperature needed to liberate it.

The ion exchange column used to analyse aqueous extracts of the lunar samples was capable of detecting as little as 5×10^{-11} mol of amino-acid. As it turned out, all the amino-acids detected were present in quantities less than 8×10^{-11} mol per gram of extract, except for glycine. Glycine, aspartic acid, glutamic acid and serine were the most abundant of the amino-acids detected. Tests on parts of the surface of one of the astronaut's gloves revealed no amino-acids, indicating that those detected did in fact come from the Moon.

compared with 1.6 to 1.7 km s⁻¹ for the overlying sediments) which has been mapped in many other regions of the Red Sea. But an even more interesting correlation can be made outside the area. Ross and his colleagues find that the Red Sea evaporites, dated by fossils in the interbedded shales, are of the same age as those previously discovered by deep drilling in the Mediterranean. They thus equate the age of the Red Sea reflector S with that of the Mediterranean reflector M.

The correlation of the evaporite surface with the widespread reflector S, backed up by direct access by drilling at other sites, implies that most of the Red Sea is underlain by late Miocene evaporites, the chief exception being the central rift valley. Ross *et al.* also find that the depth of the reflector S coincides with the depth of the brine interface in the Atlantis II Deep. This leads them to suggest that an occurrence of brine is possible wherever the evaporite outcrops in the vicinity of an enclosed basin and thus to predict the presence of other brine pools in the Red Sea. At the time that Ross and his colleagues were preparing their report, evidence for brine pools outside the Atlantis II area was scanty; but before the report had appeared, Backer and Schoell (*Nature Physical Science*, **240**, 153; 1972) had already reported the discovery of no less than thirteen new brine pools.

The widespread occurrence of late Miocene evaporites in the Red Sea also has important implications for seafloor spreading in the area. The evaporites are apparently absent from the central rift valley, but the new drill hole at site 227 showed that rocks as old as or older than Miocene occur within 1 to 3 km of what is thought to be an actively spreading ridge. This would seem to destroy the idea that spreading in the Red Sea has been continuous since a supposed beginning during the Tertiary. The most reasonable conclusion based on the data from site 227 is that the present phase of spreading began less than two million years ago following a hiatus which may have lasted since the early Miocene.

The other principal Red Sea theme is, of course, the occurrence of mineral deposits within the sediments. At site 225, dark shales were found to contain over 5 per cent iron, about 1,000 p.p.m. vanadium and about 500 p.p.m. molybdenum. Thin shale layers within the evaporite also contained 200 p.p.m. copper. Drilling at site 226 in the Atlantis II Deep was not entirely successful because of the presence of a shallow impenetrable layer of basalt. These basalts were mineralogically similar to deep oceanic tholeiites. Their metal contents were not significantly different from those of other basalts; but 14 m of sediments enriched in heavy

metals were recovered from above the basalt layer, and these may continue beneath. Site 227 (about 3 km east of the end of the Atlantis II Deep) also produced shale layers rich in vanadium and molybdenum, and copper concentrations were as high as 700 p.p.m. Ross and his colleagues suggest that these sediments could be the source of the metals in the hot brine deposits.

Site 228, near the axial valley but well away to the south-east of the Atlantis II Deep, gave sediment sequences similar to those at 225 and 227. Anhydrite was reached at a depth of 280 m but problems led to the abandonment of the hole before halite was reached. Ross *et al.* conclude, however, that halite lies within a few tens of metres from the bottom of hole 228. At sites 225 and 227, the salinity of the interstitial waters in the sediment was found to increase on approach to the evaporites to a value fairly close to that of a saturated sodium chloride solution. The assumption that a similar phenomenon applies in the vicinity of site 228 allowed the prediction of the depth of the halite. But perhaps of greater importance was the discovery of black shales containing high concentrations of zinc in the range 0.5 to 5.0 per cent. Thus in the Red Sea there are at least two suites of metalliferous shales—one enriched in vanadium and molybdenum and the other in zinc.

Hiatus Ahead

RECENT measurements at CERN confirm that the probability of interaction of a proton with another proton increases with energy up to at least 1,500 GeV. This could have serious implications for the Pomeranchuk theorem, one of the central tenets of high energy physics, which predicts that the probability (or cross-section) of proton-proton interactions will be almost the same as, or slightly less than, the cross-section for interactions between protons and antiprotons.

But the evidence so far indicates that the cross-section of the proton-antiproton interaction declines as the energy increases, certainly up to 50 GeV, the present limit of measurement. Unless this cross-section begins to increase with energy quite suddenly at above 50 GeV the inescapable conclusion is that the Pomeranchuk theorem is seriously contravened at energies of a few hundred GeV—in other words, the Pomeranchuk theorem is threatened because an extrapolation of existing data strongly suggests that the proton-proton cross-section is much higher than the proton-antiproton cross-section at high energies.

This concern about the validity of the Pomeranchuk theorem arises from two

Movement of Atmospheric Carbon Dioxide

THE variations in carbon dioxide levels in the atmosphere with the changing season is a subject of wide interest. Until recently, however, few data were available for the Southern Hemisphere; but in 1972 the CSIRO Division of Atmospheric Physics began a monitoring programme based on the collection of samples by aircraft. In next Monday's *Nature Physical Science* (March 26) Garratt and Pearman present the first results of this programme, which cover the period May 1972 to February 1973.

Most of the samples were collected by aircraft over the sea to the south-east of Australia, and these include samples collected on the same day (or within a few days) from two or more levels in the middle and upper troposphere. From June to September, there was an average increase of CO_2 content with height of 0.4 p.p.m. between 4 and 10 km, suggesting downward transfer of CO_2; between November and February (summer) there was a similar decrease with altitude, suggesting upward transfer (see figure). These patterns can be correlated with changes in the surface temperature of the sea, which decreased from May to September and increased between November and February, at an average rate of 1° C a month in each case.

Colder water has a greater capacity to dissolve CO_2 than warmer water, so

these results fit into the pattern which might have been expected, namely that gas is dissolved and then given up. This presumably applies throughout the Southern Hemisphere, at least at middle latitudes, thus explaining the seasonal variations of the CO_2 gradient from the ocean surface to the tropopause.
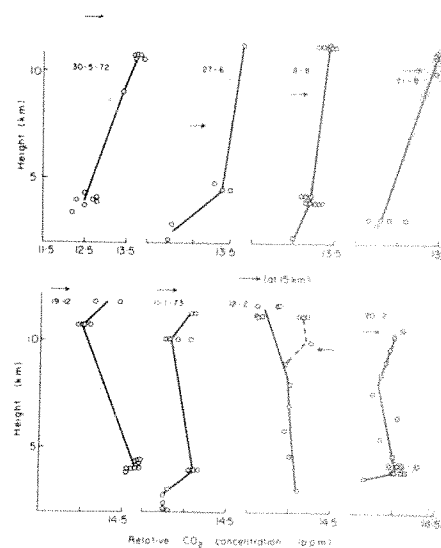
Typical measurements of CO_2 concentration at different altitudes southeast of Australia. The dates of the measurements are included; the level of the tropopause is marked by an arrow in each case.

experiments carried out at the Intersecting Storage Rings by groups from Italy and the United States and members of the CERN staff; these are to be published shortly in *Physics Letters*. What these experiments have shown is that the proton-proton cross-section increases between equivalent incident proton energies of about 70 GeV and about 1,500 GeV. A year or so ago it was confidently expected that the cross-section would remain constant in this energy range. But it now seems that the total cross-section goes up from 38 mb (38×10^{-27} cm²) at 70 GeV, to 39 mb at 300 GeV, 40.5 mb at 500 GeV and 43.2 mb at 1,500 GeV.

The total cross-section for protons interacting with antiprotons, on the other hand, is known to be more than 50 mb at 10 GeV but only 43 mb at 50 GeV. If this downward drift continues—and a definitive statement about this will have to await the results of experiments at the large accelerator at Batavia, Illinois, and at the 200/400 GeV synchroton now being built at CERN or the availability of stored antiproton beams at the CERN Intersecting Storage Rings—the Pomeranchuk theory will have to be re-examined.

VOLCANOES

Model of Etna

THE eruption of Mount Etna in 1971 is the subject of a recent issue of the *Philosophical Transactions of the Royal Society*. The diagram shows the prob-
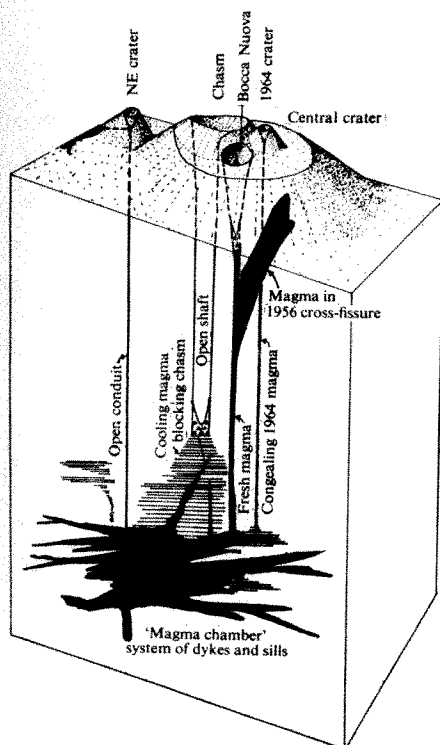
Hypothetical block diagram of the summit cone during 1971. Vertical distances are not necessarily to scale. (From Guest, *Phil. Trans. Roy. Soc. Lond.*, **A274**, 75; 1973.)

able distribution of magma within the summit cone in 1971 and provides an explanation of how the eruption came about.

The Bocca Nuova opened up in 1968 as a small gas vent and Guest (*Phil. Trans. Roy. Soc.*, **A274**, 63; 1973) suggests that it was the collapse of the Bocca in 1970 which gave rise to the 1971 eruption. The magma column below the Bocca may have burst into a fracture created during the 1956 eruption, which may then have been enlarged as a prelude to the escape of lava from the far side of the summit cone at the start of the 1971 eruption.

SEMICONDUCTORS

Low Light Levels

from a Correspondent

BECAUSE the eye, an instrument weighing 20 g and parallel-connected to an adaptive computer and several servosystems, can detect 10^{-16} W in unit bandwidth (noise equivalent power, NEP), it might be claimed that there is nothing left to do. But in an introductory review at a meeting of the Electronics Group of the Institute of Physics at Imperial College, London, on February 23, Dr T. S. Moss (Royal Aircraft Establishment, Farnborough) pointed out many deficiencies in this line of reasoning. There is, for example, ten times more radiation at 1 μm on a clear moonless night than at 0.5 μm, where the eye's response peaks, and a hundred times more (10^{-8} W cm⁻² sr⁻¹ μm⁻¹) at 1.6 μm; also the eye has a slow response and gives little range and velocity information. Furthermore, when external sources of illumination cannot be used, imaging can be accomplished in the 8 to 14 μm atmospheric window by making use of the heat of objects at ordinary temperatures, generally using cooled detectors. The need to know range and velocity has led to the development of yttrium–aluminium–garnet (YAG) lasers at 1.06 μm, carbon dioxide lasers at 10.6 μm and fast sensitive detectors.

Unequalled detectivity at 10.6 μm (the figure of merit $D^* = 10^{11}$ in a 60° field of view, twice the limit imposed by illumination from an unrestricted room temperature background) was claimed for liquid nitrogen-cooled photovoltaic diodes made from the alloy lead–tin–telluride, by Dr T. J. Waterfield (The Plessey Co. Ltd). Noise sources in these detectors and their associated amplifiers were discussed, and it was revealed that integrated arrays of detectors give uniform spectral response when used with current amplifiers. Almost as high a detectivity ($D^* = 7.3 \times 10^{10}$ in a 30° field of view) has been found in photodiodes in cadmium–mercury–telluride at 10.6 μm and this work was described by Dr J. Marine

(French Atomic Energy Commission, Grenoble) in a joint paper with Dr Motte (Société Anonyme de Telecommunications). The diodes are produced by the implantation of 250 keV aluminium ions and their subsequent annealing to give donors: the abrupt junctions have a higher quantum efficiency (50 per cent) than diffused diodes and give cut-off frequencies of 300 MHz.

Both these kinds of diode had been used by Drs C. T. Elliott and D. J. Wilson (Royal Radar Establishment, Malvern) to detect CO_2 laser radiation in a heterodyne (or strictly homodyne) system. The use of a local oscillator removes the noise from the incoherent background radiation and with a lead–tin–telluride detector a record 5×10^{-20} W, only 2.5 times the theoretical limit set by photon noise, was needed to give unity signal-to-noise in unit bandwidth (NEP); the photovoltaic cadmium–mercury–telluride detector is only a factor of two worse but holds greatest promise for the largest bandwidths. Both photovoltaic and photoconductive cadmium–mercury–telluride detectors (from Mullard) show serious non-linearities but the latter have yielded an NEP of 10^{-18} W at 193 K, thus avoiding nitrogen cooling.

Advances in photocathodes using single crystal semiconductors were described in papers from Services Electronics Research Laboratory (SERL) and Mullard. Dr G. A. Allen described how the devices depend on obtaining a p-type semiconductor in which the bottom of the conduction band lies above the vacuum level, that is with negative electron affinity. This is achieved by coating the semiconductor surface with caesium and oxygen, which provides a thin positive space charge through which minority carriers tunnel into vacuum. In a transmission photocathode light must penetrate through a transparent medium, which forms the wall of the vacuum chamber, into an active region, usually p-type gallium arsenide a few microns thick. In order to avoid loss of minority carriers at dislocations the transparent substrate must be a crystal of matching lattice parameter. The growth of both substrate and layer by liquid phase epitaxy was described by Dr M. C. Rowlands. Their much higher quantum efficiency will probably make such photocathodes standard devices for the near infrared.

Three of the contributors dealt with detectors based on silicon technology; Dr J. M. Shannon (Mullard) described arrays based on photosensitivity junction field-effect transistors, Dr J. Dickson (Plessey) discussed limitations of arrays in general, and Dr R. Webber (SERL) discussed the theory of photodiodes operating under avalanche conditions.

Science for the Public Service

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This article is based on a speech delivered by Sir Alan to the Parliamentary and Scientific Committee at its annual luncheon on February 8, 1973.

WE have just benefited from a great national debate on the organization of applied research and development. There have been government papers, both green and white, reports by the Select Committee on Science and Technology, Parliamentary debates, and innumerable comments and articles. It has been a frank and lively discussion and I am told that we have been envied abroad by people who wish it were possible to hold a similar public airing of scientific policies in their own countries. Now that the debate is over, I believe everyone will benefit if we can achieve what the government has consequently set out to do, which is to bring closer together the people whose job it is to know the practical problems to be solved and those whose job it is to know what research is necessary to solve them and how to do it.

Balance

A good debate, yes ; but I think it has involved some risk of getting things out of balance. We must always remember, for example, that research and development are only a part of the total scientific and technical activity of the country and occupy only a fraction of the scientific manpower. Most of the qualified scientists and engineers in industry are not doing research and development at all ; they are managing, designing and looking after technical marketing and sales, which are all necessary to realize the material benefits of science and technology. Even in government, research and development are, together, only one of various scientific services. There are many others: for example, weather forecasting, operational analysis, setting and maintaining standards, surveying and mapping, monitoring of public health and pollution, testing of foodstuffs, chemical analysis, forensic science, and diagnosis of causes of accidents. Only occasionally does this kind of work make the headlines, as, for example, in the investigations of the Ronan Point and Comet aircraft disasters, or the recent identification of swine vesicular disease, but it is nevertheless work that is greatly satisfying in both its intellectual content and its contribution to public services.

Quality

A second possible risk in the debate—that of raising doubt about the quality of the research and development work—fortunately did not emerge at all. For it to have done so would have been quite without justification. The government's concern in fact was entirely with questions of organization and in particular with how to bring those who do the research and development closer to those who need its results. The high quality of the work itself was never in doubt, and we have only to look at a few recent successes to see how good it is.

The blind landing equipment pioneered by the Royal Aircraft Establishment and taken up by our industry is proving to be a world winner and is now going into many types of civil aircraft which have been accepted for automatic landings. Again, the gas centrifuge process which we have developed for enriching uranium, this time with our German and Dutch partners, is also looking most promising for commercial operation. The Advanced Passenger Train, the carriages of which have a most clever suspension system that enables them to run smoothly at great speed on ordinary track, is ahead of anything else of its kind in the world ; and because the most common transport facility that most countries have is a network of ordinary railway lines, this train should attract worldwide interest.

Sir Alan Cottrell, Chief Scientific Adviser to the government.

Similarly in many other fields. For example, in the use of very large computers for weather forecasting ; or the development of carbon fibres and other new constructional materials ; or equipment for the dispersal of oil at sea, which has been exported all over the world. We have also developed a narrow-beam long-range asdic for exploring the ocean floor ; and in the transport field, the high-temperature sodium-sulphur battery for electric propulsion is promising. There have been some striking advances made in the rearing of fish and shell-fish and this country is well advanced in the experiment of producing protein from oil by micro-organisms, as also with synthetic "steaks" from high-protein beans. We have developed some highly successful new varieties of winter wheat, which are now being exported as well as widely used in this country. The application of

clinical epidemiology to the evaluation of health care is another important advance. In yet another field, the first systematic national air pollution monitoring system in the world, developed by the Warren Spring Laboratory, has provided a model which has been copied by several other countries.

Improvement

These are just a few of our recent scientific and technical successes. There are many more. For a country of our economic size it is, I think, a very creditable performance. Can we do even better? Yes, I think we can, by achieving even closer understanding between the researcher and the user, and this is one of the reasons for our reorganization. One pitfall which we must avoid, of course, is the temptation to spread our efforts too thinly. To pioneer a new technology is expensive and we must be on our guard not to embark on glamorous and costly developments simply because they are fashionable. We also have to exert self-control in limiting ourselves only to those projects which are within our means. The newly-formed Requirements Boards will have an important part to play here, so far as governmental projects are concerned. Because we cannot afford to compete in every field the answer will sometimes lie in joint ventures with other countries; and our entry into the European Economic Community should, of course, do much to stimulate these.

One of the chief purposes in all this is the economic welfare of the country, but there is, I believe, a basic misconception when people try to relate our research and development efforts to the economic condition of the country. One of the clichés of the time is the remark that Britain is one of the heaviest spenders on research but has one of the most slowly growing economies. This is supposed to be a great mystery and paradox. But the answer is simple. Research and development can achieve great technical miracles but cannot by themselves achieve great economic miracles; for these you must also have the massive capital investment in the new industrial plant and equipment needed to embody the fruits of research and development in actual production. Research and development may be spark-plugs of the economy, but only when they are attached to an engine can you get power.

The achievement of economic growth thus lies beyond research and development itself and is a matter of investment in productive plant, which may be used for new industrial ventures made possible by that research and development. Investment, of course, raises other problems; and we are making a great effort at present to break through the stranglehold of low capital investment and low growth without running into excessive inflation and balance of payments problems. The government's recent decisions to give massive financial support to the coal and steel industries show some of the determination here. We all look forward to the success of these efforts.

Widening Horizons

If we now expand our view in space and time, extending it to Europe and to the world as a whole, the problem of generating sufficient investment capital seems likely to grow more general and more severe in the years to come. In developing countries it is already the chief factor that limits their ability to raise their standard of living by creating more jobs, and installing much needed power stations, desalination plants, and other vital equipment. In the industrialized countries it will become critical in the final years of this century for meeting the future requirements for energy and raw materials. Western Europe and Japan are already the world's biggest importers of these and their needs are con-

tinuing to rise in the face of a world situation where raw materials are being increasingly consumed, where the bargaining strength of producer countries is growing, where the United States itself is beginning to become a major importer of the same materials, and where protection of the natural environment is an increasingly important constraint. In the past, technological advance in the mining and minerals industries has been able to keep prices of basic resources fairly steady, in the face of the changing demand–supply situation, but it will be pretty hard put to keep up this balance in the future.

In a strictly scientific sense there is no possibility of running out of material resources. The point is that it will cost more and more to continue to meet our needs. At much higher extraction costs, vast reserves of oil in the tar sands and shales could be tapped. Aluminium could be extracted from clay, uranium from granite and water could be desalinated. Given the money, all these and many other things could be done, including improvements to the environment. We could provide our houses, for example, with district heating from waste sources. Or fit them out with heat pumps; or solar heaters; or fuel cells running on hydrogen made at nuclear power stations hundreds or thousands of miles away. We could carry our electricity along underground superconducting cables. We could use other means of propulsion for motor vehicles. But the overall limiting factor will be availability of capital. To take just one item as an example, a recent forecast is that this country will need 100,000 MW of nuclear electricity by the year 2000. That will mean spending nearly £1,000 million a year on nuclear plant alone once that programme is fully under way in the 1980s and thereafter.

New Technologies

These are very broad issues, of course, and will involve high policy in the European Economic Community. But research and development will have important parts to play. Improved mining techniques, the intensification of scrap recovery and recycling, the development of substitute materials, will all help to ameliorate the resources problem but each will require considerable scientific and technical effort. Whichever way these new technologies develop, it seems almost certain that they will cost more in energy to run, so that eventually the most critical thing of all will be the supply of energy. The extent to which national policies in such common fields as energy and the environment are to be coordinated in West European effort must obviously be a matter for detailed discussion within the EEC. At present we are, of course, in a good position in Britain with our coal reserves, North Sea discoveries, and nuclear developments; but looking further into the future and also to our position as a member of the European Economic Community, this is no time for complacency. The government in fact has already stressed this in its decisions to develop strong capabilities for the future in the coal and nuclear fields. It will, of course, be essential to back these decisions with strong scientific efforts, and at the same time to press forward generally with the exploration of ways of providing and using energy more efficiently and economically.

Not only are there many opportunities here for science and technology to make great contributions to the country's future well-being and to that of the European Economic Community as a whole, but it will in fact be essential to harness science and technology to do so. This is a great challenge to the whole scientific community, but my experience of government laboratories, of the research councils, industry and the universities leads me to the view that our scientists and engineers will respond to it just as willingly, as enthusiastically and as effectively as they did in the most memorable past.

Controversy about MIRVs

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> The debate about how successfully the Soviet Union could eliminate United States land-based missiles with its own SS-9 launchers seems to turn on how many 1 Mt warheads the Soviet device could carry.

IN the course of the public debate in the United States on the decision to deploy anti-ballistic missile defences, a sharp, and in some cases acrimonious, disagreement emerged between those expert witnesses who contended on the one hand that the Soviet Union would by some near future date find little difficulty in employing its offensive missile forces to destroy up to 95% of the American land-based offensive missile force, and on the other those who saw great difficulties which would prevent the Soviet Union from ever becoming capable of such a thing. The latter, and probably more numerous, school found its most articulate and consistent spokesman in Professor G. W. Rathjens, whereas the former found its champion in Professor Albert Wohlstetter.

Disagreement

The gulf of genuine disagreement between the two schools appeared so great, in spite of the considerable measure of common understanding that had been reached by their principal spokesmen, at least, on the presumed values of the physical characteristics of the Soviet missile force—its size, accuracy and overall reliability were not, ultimately, in dispute—that the Operations Research Society of America (ORSA), at Wohlstetter's request, conducted an enquiry into the affair. The results of the enquiry were published in September 1971 (ref. 1) and came down very much on the side of the Wohlstetter school. But the publication of the enquiry's findings, and, indeed, the manner of the setting up of the enquiry, have led to a new controversy, part of which is reflected in a selection of letters published by the ORSA in January 1972 (ref. 2).

One remarkable feature of the original debate, as it was recorded in oral and written testimony before the United States Senate[3] and elsewhere, and of the ORSA enquiry, was a steady refusal to state and analyse the problem in general terms, partly, no doubt, in the former instance because of reluctance to alienate a non-mathematical audience and partly, presumably, because of worries that information of a "classified" nature (available, it seems, to both Wohlstetter and Rathjens, if not to all their supporters) could be inferred from an analysis conducted this way. (All subsequent references to the Wohlstetter and Rathjens positions relate to testimony and papers published in ref. 3 unless otherwise stated.)

This practice, however understandable in some ways, has had several undesirable consequences for a debate of such wide public and political concern. Contentious calculations have been conducted without the basic assumptions being exposed to view; the use of secret data to arrive at public conclusions has made it all but impossible for an intelligent outside observer to decide where the truth lies when conclusions differ; and the relative importance of the physical parameters involved, insofar as uncertainties in knowledge of their values affect the general precision and trustworthiness of the conclusions reached, has been left obscure. In an attempt to redress some of these failings, what follows is a general analysis of the problem, conducted in simple terms and, partly from necessity but also because of the openness it allows, based only upon publicly available data. The intention is to expose the structure of argument upon which all conclusions about this problem must ultimately rest. It is not intended, however, to present numerical conclusions of superior accuracy to those of either school; rather I shall show how reliable conclusions may be reached, given a knowledge of the key parameters, and demonstrate that some uncertainties are likely to persist no matter how trustworthy this knowledge is.

Probabilities

To begin with, it is necessary to establish the probability, p_k, that one perfectly reliable missile warhead (one of many presumed identical missile warheads whose accuracy is known on a statistical basis) aimed at a concrete emplacement (taken to be a point target) will so damage the emplacement as to render inoperative the missile launcher contained within it. Assuming that the theoretical distribution of miss distances of an infinite number of shots at the emplacement would be normal, and recalling that military usage ascribes accuracies to projectiles on the basis of their "circular error probable" (CEP)—the radial distance from the target within which half of an infinite number of shots fall—it follows that

$$p_k = 1 - (\tfrac{1}{2})^{L^2/C^2} \tag{1}$$

where C is the CEP and L the distance from the target within which the warhead must explode in order effectively to destroy the target. L is related to the explosive energy yield of the warhead, Y, and the critical blast pressure under which the concrete emplacement will start to collapse, T, by

$$L^3 \propto Y/T \tag{2}$$

Missile warheads are, however, known not to be perfectly reliable; rather they will in general only have a definite probability (determined by test programmes of one kind or another) of reaching the target area once the decision is taken to launch them. If the probability of a missile warhead reaching the target is p_r then the overall probability that the target will be destroyed becomes $p_r p_k$. If the missile warheads are arranged to be aimed n to a target, the overall probability of the target being destroyed becomes $1 - (1 - p_r p_k)^n$. Or, put slightly differently, the expected fraction of targets surviving an attack of n missile warheads a target is

$$(1 - p_r p_k)^n \tag{3}$$

Alternatively, if those controlling the attack have perfect information as to which of their missile warheads will fail to reach their target and are able to stagger firings to permit the

substitution of additional launchers (and reprogramming of guidance systems), the expected fraction of targets surviving an attack by the same number of missile warheads as before becomes less in general, namely $(1 - p_k)^{np_r}$. The difference between this expression and expression (3) is rather small for large n and small p_k, but becomes significant for small n and large p_k.

In practice, those responsible for the attack cannot be expected to possess perfect information about which of their missile warheads will malfunction—at any rate not soon enough to take full advantage of the knowledge. If p_r^0 is the probability that a missile warhead will prove reliable during that phase of its trajectory about which those in control of the attack have no useful information, the expression for the expected fraction of targets surviving the attack becomes

$$(1 - p_r^0 p_k)^{np_r / p_r^0} \tag{4}$$

(And in the event, more likely than not, that the exponential term in this expression is not a whole number, the best strategy for the attacker is to allocate the nearest lower whole number of missile warheads to all targets and one extra missile warhead each to as many targets as possible.)

Numerical values can now be attached to the various parameters involved in the solution of the practical problem, around which the controversy revolved, of the survivability of the 1,000-strong US land-based Minuteman force in the face of a hypothetical Soviet attack force of 500 SS-9 missile launchers, each capable of carrying several warheads (in multiple independently targetable re-entry vehicles, MIRVs). This statement of the problem is common ground to Wohlstetter and Rathjens; I shall ignore for the moment the fact that the Soviet Union has recently agreed to restrict its SS-9 forces to below 500.

The value of p_k depends, as outlined above, on three factors: the warhead CEP, the yield of the warhead and the "hardness" or blast resistance of the concrete Minuteman emplacement. Both schools agree about the probable value of the CEP of the SS-9, but neither publicly specify it. A rounded figure well inside theoretical limits[4] and near the published guesses would be 460 m (0.25 nautical mile): and one can expect military planners to be confident of the CEP of their warheads to within plus or minus 30 m or so[4]. Rathjens performed his calculations exclusively on the basis of a warhead yield of 1 Mt (TNT equivalent) and Wohlstetter worked on the basis of two possible yields, 1 Mt and 5 Mt, while judging the latter to be the more relevant. The blast resistance of the Minuteman emplacement I shall take to be 300 pound inch^{-2}, which has been cited as a plausible figure for some years now[5] and may well be below what can be achieved—however, p_k does not depend as strongly on blast resistance as on CEP. Wohlstetter and Rathjens do not publicly specify blast resistances, except that Rathjens's estimate, according to Wohlstetter, was two-thirds higher than his own. Obtaining p_k from standard graphs[6] of accuracy/yield relationships, it turns out that

$$p_k(5 \text{ Mt}) = 0.98 \pm 0.01 \text{ and } p_k(1 \text{ Mt}) = 0.77 \pm 0.04$$

where the error estimates arise from probable uncertainties in CEPs.

Reliability

According to Wohlstetter the same overall SS-9 reliability probability, p_r, was assumed by himself and Rathjens: he does not specify its value. The ORSA conducted a calculation on the basis of $p_r = 0.73$—a seemingly somewhat arbitrary figure. The firmest and most authoritative public estimate of p_r made

before the debate was that of Fink[7]. He put $p_r = 0.66$ for the United States's own pre-MIRV warhead missile forces. For the SS-9 force I shall use the rounded figure of 0.7, to take some account of possible improvements since Fink's article was published. (Fink's figure was for the United States retaliatory force and it might be said that for a force used to initiate a conflict the overall figure should be higher—given that surprise is on the side of the attacker. This may be true, but it should be noted that even small temporary delays in "countdown" could seriously interfere with the side contemplating surprise attack using staggered firings, whereas these would scarcely matter for a retaliatory strike.)

This overall probability can be seen as a product of four contributing factors[7]: (i) the probability that the missile launchers are available; (ii) the probability that they are ready; (iii) the probability that they complete boost phase reliably; and (iv) the probability that the payload is reliable in the post-boost phase.

If all these four probabilities are taken to be equal, they will each have a value of 0.91. In practice, however, it would be surprising if the first and second of these probabilities were not somewhat larger than this average figure, given that an attacker can choose to make his attack when circumstances most favour him. And it would be equally surprising if the last of the probabilities were not somewhat smaller than the average, given the relatively complex engineering system associated with a multiple warhead payload; in any case, the value of the post-boost phase reliability probability cannot be as well known by those planning an attack as the values of the first three, even when multiple warhead payloads are commonplace, because the Partial Test Ban Treaty prohibits full (complete with warhead detonation) flight testing of missile warheads.

Rather than treat the four probabilities as equal, as does Fink (the ORSA report put the first two equal and high, 0.95, and the last two equal but slightly lower, 0.90), it would seem a slightly better approximation to the actual situation to assume that planners might tend to assign equal values to the first two (0.95), and 0.91 to the third—all fairly firmly—and a smaller and less precise estimate (0.86 ± 0.05) to the fourth. (Fink[7] suggests that a conservative military planner might attach a 10% downwards uncertainty to each of the four reliabilities: placing a 6% error bracket on one of them only does not by comparison seem to be ascribing an unusual degree of caution.)

Throw-weight Capability

It now remains to establish how many separately targetable 1 Mt warheads a MIRV SS-9 can carry. Official US spokesmen claim that the SS-9 can launch either one 25 Mt warhead or three 5 Mt MIRV warheads[3]: these figures, and, presumably, the booster capacity implied, were never disputed in the debate. Rathjens, however, suggests that the SS-9 could, alternatively, carry four 1 Mt MIRV warheads, but Wohlstetter (and the ORSA) insist that this is too few, without actually making explicit what they regard as the true figure. An independent estimate can be made with the help of some simple calculations. If, as is usual *, the weight of a warhead is assumed to depend upon the yield raised to some power, the above official data suggest a two-thirds power law, which when applied to the 1 Mt case indicates that an SS-9 launcher is capable of a payload of nine 1 Mt MIRV warheads. But this sort of calculation ignores the weight of the post-boost phase missile warhead release system which is part of all MIRV payloads. Applying the two-thirds power law to the known case of the conversion of the United States Minuteman II launcher from a payload of 2 Mt to three MIRV missile warheads of 0.2 Mt each, the weight of the warhead release system

* See, but for a different power law, Kent[8]. According to the ORSA[1], Rathjens also employed a power law approach to this question.

for three 0.2 Mt warheads comes out as equivalent to that of two extra 0.2 Mt warheads. If the weight of the Soviet SS-9 warhead release system per warhead in excess of unity can be taken to be the same, then that for six 1 Mt warheads would weigh roughly as much as two extra 1 Mt warheads (but the mechanism for three 5 Mt warheads only as much as 0.25 extra 5 Mt warheads). Seven then seems a more plausible figure than that of Rathjens, or that resulting from a crude application of the two-thirds power law, for the number of 1 Mt MIRV warheads an SS-9 could carry.

It is now possible to tackle, but in an open manner, the various calculations performed by Wohlstetter, Rathjens and the ORSA. Taking the number of US missile emplacements to be 1,000 and the size of the Soviet SS-9 attack force to be 500 launchers (or its equivalent: one of the recent strategic arms limitation agreements puts an upper limit of approximately 300 on the SS-9 force until 1977 at least) and assuming first of all no Soviet ability to substitute for failures, expression (3) predicts that the percentage of US missile launcher emplacements likely to survive might be taken by Soviet planners to be $7 \pm 2\%$ for a 1 Mt SS-9 MIRV force ($p_k = 0.77 \pm 0.04$, $p_r = 0.7 \pm 0.04$, $n = 7$). For a 5 Mt SS-9 MIRV force ($p_k = 0.98 \pm 0.01$, $p_r = 0.7 \pm 0.04$, $n = 3$), the surviving fraction becomes $20 \pm 2\%$. Wohlstetter gives 7.3 and 16%, respectively; Rathjens gives 25% for his 1 Mt SS-9 (four warhead) MIRV attack, the ORSA does not investigate the non-substitution possibility.

On the other hand the assumption could be made, possibly more realistically, that the Soviet Union will be able to substitute for failures up to and including, but not beyond, the booster separation stage, which is reached about 5 min after launch and after the launcher has travelled approximately 1,000 km of its flight for a missile launcher of the SS-9 type[4] (indeed all indicators suggest that the United States is itself currently unable to substitute for failures of this type). Under these circumstances expression (4) yields $5 \pm 2\%$ for the fraction of US missile emplacements which the Soviet Union may expect to survive its attack with a 1 Mt SS-9 MIRV force ($p_k = 0.77 \pm 0.04$, $p_r = 0.7 \pm 0.04$, $p_r^0 = 0.86 \pm 0.05$). For a 5 Mt SS-9 MIRV force ($p_k = 0.98 \pm 0.01$, $p_r = 0.7 \pm 0.04$, $p_r^0 = 0.86 \pm 0.05$) the survival rate becomes $12 \pm 4\%$. Wohlstetter gives a bald 5% for both cases; the ORSA gives 5% for the 5 Mt SS-9 MIRV case on the basis (like Wohlstetter, presumably) not only of a higher overall reliability than that assumed here but also of an assumed Soviet ability to substitute for some (50%) of its post-boost phase failures. Rathjens does not consider the possibility of failure substitution. It should be noted that the fraction of missile emplacements surviving an attack is not the same as the useful surviving percentage of missile launchers; this is less by a factor of 0.70, in our case, to allow for unreliability.

Implications

Several points of general interest emerge from the above. First, uncertainties as to CEP values are relatively unimportant for high p_k values, that is for large yield missile warheads; a 6% uncertainty in CEP contributes only a 1% uncertainty to p_k for a 5 Mt warhead but a 5% uncertainty to p_k for a 1 Mt warhead. It follows that Wohlstetter's insistence in the debate on the importance of missile warhead accuracies and the likelihood of their improvement; thus, he alleged, placing Minuteman emplacements even more at risk was just a little beside the point, particularly in the context of a discussion centring on 5 Mt warheads which Wohlstetter contended was the most realistic case: a p_k of 100%, together with the values for the SS-9 reliability factors quoted above, would still result in 11% of Minuteman emplacements surviving a 3×5 Mt attack. The non-substitutionable failure rate, not the accuracy, is the important limiting factor here. For the theoretically possible 7×1 Mt case, uncertainties in non-substitutionable failure rate and in CEP contribute about equally to uncertainties in the final result.

This hitherto relatively unsung importance of reliability, it might be noted, places the significance of the Partial Test Ban Treaty as an arms limitation agreement in a much more favourable light than it has recently enjoyed.

Second, it follows that placing a single figure without error brackets on the survivability rate, as seems to have been the habit of all parties concerned in the debate, is an almost meaningless activity. (Wohlstetter seems to have been the worst offender here; at one point[3] he quotes a survivability rate to an implied accuracy of 1 to 2%.) It seems a fair presupposition that military planners responsible for analysing the consequences of attacks of this sort will not be in possession of precise figures for the reliability and accuracy of their forces, and that a prudent planner contemplating attack will be more influenced by the upper limit of his estimates of emplacement survivability than the lower. It is typical of calculations of this sort, of course, that a planner contemplating defence might consider it prudent to concentrate on the lower limit of survivability—an example of the so-called "worst case analysis" ascribing to an adversary, without any apparent justification, capabilities that the adversary himself could not prudently rely on.

Third, it turns out that the above numerical conclusions, although not based upon much more than rough estimates of some parameters, broadly speaking agree more closely with those of Wohlstetter than with those of Rathjens, at least insofar as they indicate that the fitting of multiple independently targetable missile warheads to land-based missile launchers will reduce to a considerable degree the relative value of these launchers as a means of retaliation to an attack designed to take advantage of their vulnerability. A pre-MIRV SS-9 force of 500 launchers would have left at least 500 Minuteman emplacements intact, whereas, according to my calculations, the same force fitted with 3×5 Mt MIRV warheads, and launched using the substitution technique for system failure as far as, and including, the boost phase, would leave at most only 160 emplacements intact, containing perhaps 110 reliable launchers—a total of 330 missile warheads. Greater reliabilities for large warhead MIRVs and their launchers, or a greater subdivision of payloads into more numerous, accurate, and reliable smaller missile warheads, would have the effect of making the trend more marked. This prospect of a gradually diminishing utility of fixed emplacement land-based missile launchers as a retaliatory force, particularly in the absence of anti-missile missile defence of emplacements, is bound further to encourage the development of new forces of a mobile and therefore less pre-targetable sort and to result in more weight being placed on the development of existing mobile types such as those based on submarines and aircraft.

And finally, although the differences between Wohlstetter and Rathjens can be regarded as being primarily differences in judgment about how Soviet weapons policy may develop, and it is too soon to say definitely who is right, it should also be noted that Rathjens's results would nonetheless not differ significantly from Wohlstetter's if his method of calculating the number of 1 Mt MIRV warheads an SS-9 launcher could carry were the same as that used here.

[1] *Operations Research*, **19**, No. 5 (1971).
[2] *Operations Research*, **20**, No. 1 (1972).
[3] *Hearings before the Committee on Armed Services* (United States Senate, April–June 1969).
[4] *Impact of New Technologies on the Arms Race* (edit. by Feld, B. T., Greenwood, T., Rathjens, G. W., and Weinberg, S.), 81 (The MIT Press, Cambridge, 1971).
[5] *Arms Control, Disarmanent, and National Security* (edit. by Brennan, D. G.), 216 (Braziller, New York, 1961).
[6] *Strategic Survey 1969*, 33 (International Institute for Strategic Studies, London).
[7] Fink, Daniel J., in *Science and Technology*, 54 (October 1968).
[8] Kent, Glenn A., *Occasional Papers in International Affairs, No. 5*, 28 (Harvard University, 1963).

Late Miocene Desiccation of the Mediterranean

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This article presents evidence that the Mediterranean Sea was a desiccated deep basin some 6 million years ago.

THE presence of an evaporite deposit of Late Miocene Messinian age under the Mediterranean Sea was discovered two years ago by the Deep Sea Drilling Project (DSDP) Cruise Leg XIII (refs. 1–4). To start with, our postulates were greeted with disbelief, but detailed analyses of samples and syntheses of regional geology during the past two years have led to a confirmation of this apparently preposterous idea. We shall present in this article our principal conclusions and some of the critical evidence. Detailed documentation will be published in due course[5].

Three Models

The origin of the Mediterranean evaporites could be accounted for by three different models. In the first, there was evaporation of a deep water Mediterranean basin, which received constant inflow from the Atlantic so that its brine level was maintained at or slightly below the world wide sea level. The second involves evaporation of a shallow water Mediterranean basin, which, similarly, received constant inflow from the Atlantic so that its brine level was maintained at or slightly below the world wide sea level. According to the third, desiccation of a deep Mediterranean basin, isolated from the Atlantic, took place, so that evaporites were precipitated from playas or salt lakes whose brine levels were dropped down to thousands of metres below the Atlantic sea level.

The first may be called the "deep water, deep basin model"[6] and the second the "shallow water, shallow basin model"[5]. The third, namely the desiccated deep basin model, is, however, the one we prefer.

Late Miocene Basin Geometry

Geophysical evidence—chiefly the basin-wide distribution of an acoustic reflector[8] (Fig. 1) which has been identified by drilling as the top of the Mediterranean evaporites[5]—clearly indicates that the Late Miocene Mediterranean had a configuration not greatly different from that of today. The surface of the reflector conforms more or less to the contours of the intricate submarine topography, indicating that the Mediterranean basin had already been created when the evaporite was being deposited.

More convincing evidence is provided by stratigraphical and palaeontological studies. The strata underlying the evaporites are deep marine pelagic sediments. During the DSDP Leg XIII, Middle Miocene pelagic marls were cored from sites 126 and 129 (see Fig. 2) in the Ionian Basin[1,5], and lower Upper

Miocene (Tortonian) marls were sampled from site 121 in the Alboarn Basin[5]. The correlative Tortonian marl underlying the Upper Miocene evaporites (Messinian) of Sicily has been proved to be a deep water deposit by a study of its benthonic foraminiferal faunas[9]. Deep marine pelagic marls of Lower Miocene age are also known on the island of Pianosa in the Tyrrhenian Sea[10]. These facts clearly indicate that the Mediterranean basins were already deep before the salinity crisis.

The strata directly overlying the Messinian evaporites are also deep marine pelagic sediments. These earliest Pliocene strata contain a benthonic ostracod fauna, which could only live in ocean bottom below 1,000 m (ref. 11). The associated benthonic Foraminifera are likewise indicative of a deep marine environment of deposition[9]. The fact that of the deep-swimming planktonic genus *Spheroidinellopsis* is the dominant (up to 90%) microfauna lends further credence to the concept of a deep Mediterranean in the earliest Pliocene[5]. Additional data in support of deep marine sedimentation immediately after the salinity crisis have been provided by the oxygen isotope measurements[5]. As geophysical considerations exclude the possibility of a catastrophic subsidence[5], the only alternative is the sudden drowning of a desiccated deep basin.

Pelagic oozes are, in fact, intercalated in the Messinian evaporites. At site 134, to the west of Sardinia, we cored a
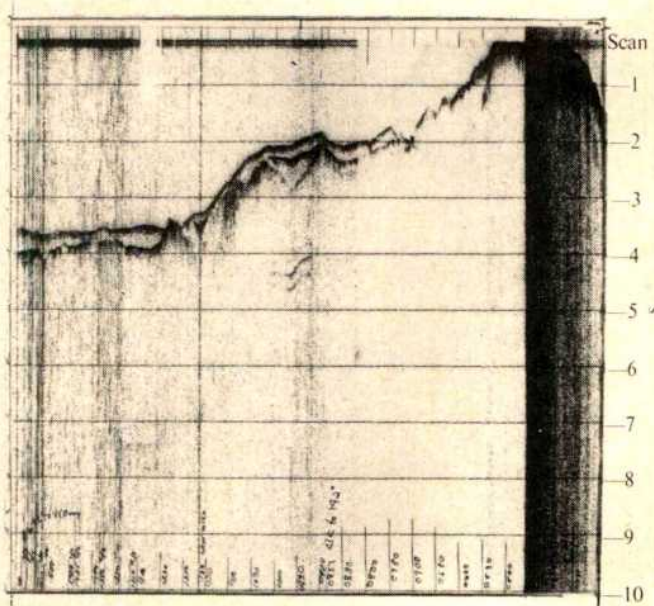
Fig. 1 The Mediterranean reflector. This strong reflector corresponds to the top of the Upper Miocene evaporite formation. The relief of the reflector conforms the bottom topography, suggesting that the evaporites were deposited in a basin similar in topography to that of the present Mediterranean.
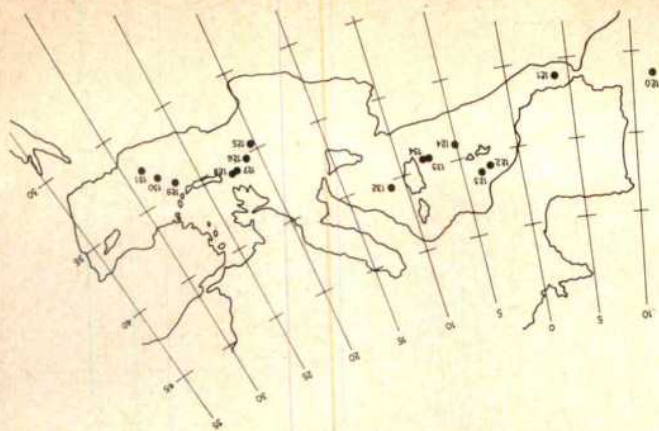
Fig. 2 Drill sites of Leg XIII of the Deep Sea Drilling Project.
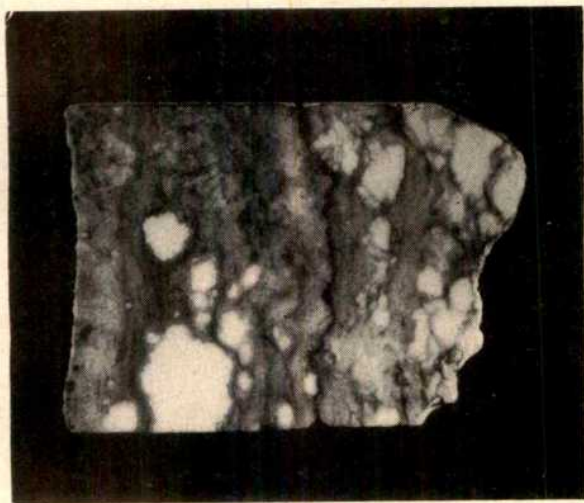
Fig. 3 Nodular and "chicken wire" anhydrite, characteristic precipitates from ground waters under hot and arid coastal flats.

deep marine foraminiferal ooze of Messinian age between two sterile halite layers[5]. Similar marl oozes have been encountered between anhydrite layers at site 124 south of Mallorca[5] and in the Messinian evaporites now uplifted and exposed on Sicily[7]. Where a Late Miocene Mediterranean basin was located near land, as in the case of Periadriatic Trough in Italy or Khania Basin in Crete, deep water turbidities are interbedded with the evaporites[12,13].

If the Late Miocene Mediterranean had been shallow, the marine sediments associated with the evaporites would have been shallow water deposits. This is not the case. The occurrence of deep marine sediments below, above, and within the evaporite sequence proves conclusively that the Mediterranean was already a deep basin during Middle and Late Miocene times.

Environment of Deposition

Although the Upper Miocene marine sediments are deep water deposits, mineralogical, petrographical, sedimentological, and geochemical data strongly suggest that the Upper Miocene evaporites were, on the whole, not precipitated from a deep brine pool; they were formed chiefly in shallow waters or subaerially.

The presence of anhydrite as a dominant sulphate mineral in the Mediterranean evaporites is a strong argument against the idea of a deep water genesis. Anhydrite, $CaSO_4$, is the higher temperature polymorph of calcium sulphate. Below a critical temperature of phase transition, gypsum ($CaSO_4.2H_2O$) should be precipitated. This critical temperature is 58° C for

the $CaSO_4.H_2O$ system[14], but is about 20° C for calcium sulphate precipitated from brines saturated with sodium chloride (ref. 14 and F. W. Dickson, personal communication). Deep aqueous bodies rarely acquire a temperature high enough to precipitate anhydrite. Even the Dead Sea, where the surface temperature exceeds 30° C and may locally exceed 40° C, anhydrite is not formed[15]; only gypsum is found on the shores and on the bottom of it.

The occurrence of anhydrite in the form of nodules proves further that it has been crystallized in a subaerial environment. Nodular anhydrite is found today exclusively on hot and arid coastal flats, called *Subkhas* in Arabic, where it is precipitated at the ground water table, 0.5 m or so beneath the surface at temperatures above 35° C (J. Schneider, personal communication); this diagenetic mineral replaces carbonates and sulphates deposited earlier and may form a whole anhydrite bed in which only wisps of organic materials remain. The resulting structure has been given a vulgar name of "chicken wire anhydrite" by geologists working in the petroleum industry and has been considered by some to be an infallible criterion of subaerial crystallization[16] (see Fig. 3).

A careful examination of the cores from site 124, to the south of Mallorca, reveals that the process of formation of evaporite there consists of several cycles of inundation and desiccation (Fig. 4). Each cycle commences with the deposition of laminated carbonates. The predominant carbonate is a dolomite rich in organic matter, and its evenly laminated structure is indicative of deposition in quiet, and probably fairly deep, bodies of water. The carbonates yield either marine micro and nannofossils, or a brackish fauna and flora; they were either
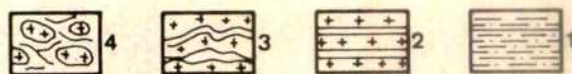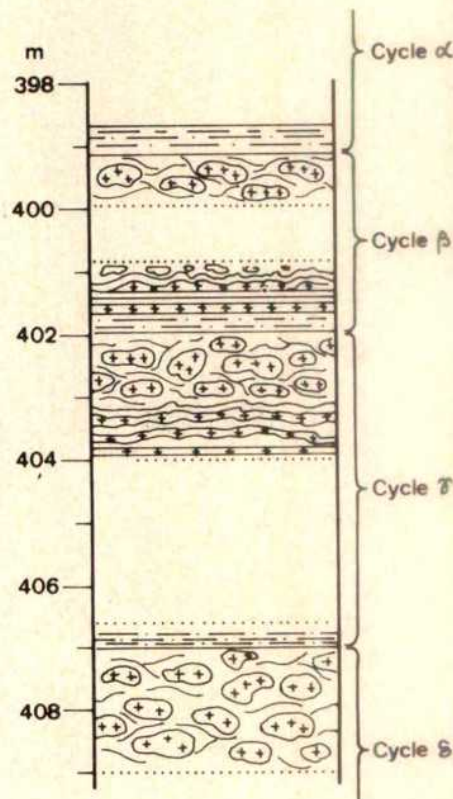
Fig. 4 Schematic diagram of desiccation cycles in hole 124. 1, Laminated carbonates; 2, interlaminated dolomite and anhydrite; 3, stromatolitic deposits; 4, nodular anhydrite.

deposited in a deep sea or in a large brackish lake. Overlying the laminated carbonates are interlaminated dolomite and anhydrite; the laminations are less well defined near the top, a trend suggestive of increasing agitation as the water became shallower. Stromatolites appear near the top of the depositional sequence; they formed only when the brine pool was sufficiently shallow to permit the growth of algae. At the very top of every cycle is the nodular anhydrite, presumably a product of subaerial diagenesis. The anhydrite is covered in turn by very evenly laminated carbonates of the next cycle of inundation.

The halite rock samples from beneath the Balearic abyssal plain also show signs of desiccation. Euhedral "hopper crystals" precipitated in brine pools have been partially replaced by anhedral clear crystals during times of subaerial exposure. A desiccation crack is present, filled with clear halite (Fig. 5). Intercalated in the halite is a cross-laminated foraminiferal silt that has apparently been deposited in an aeolian environment.

Playa deposition is further supported by investigations of stable isotopes. Fig. 6 shows the range of oxygen isotope values of the Mediterranean evaporites[17]. The great variability argues against the idea of precipitation from a brine pool. In fact, the wide range is very similar to that of the playa evaporites, by contrast with the narrow range characterizing the marine evaporites.
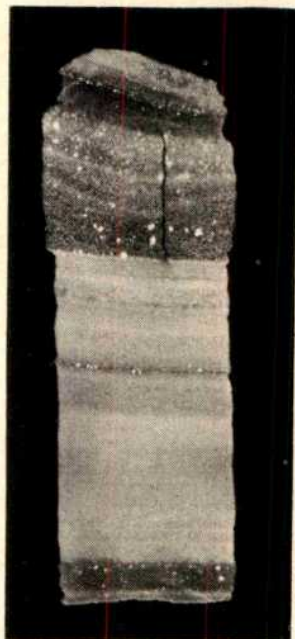
Fig. 5 Halite core from site 134.
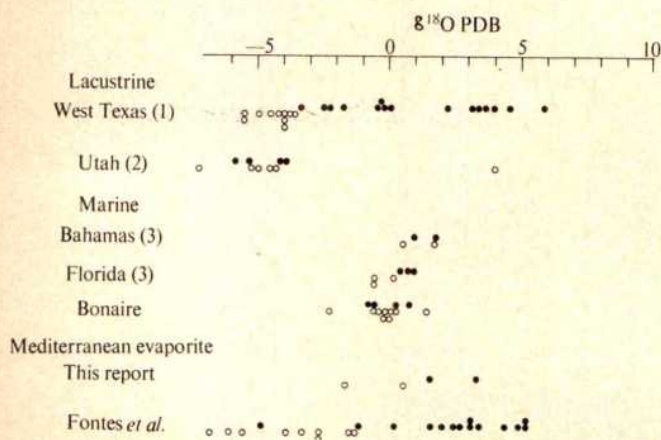
Fig. 6 Oxygen isotope range of the Mediterranean evaporites by comparison with marine and playa evaporites. ●, Dolomite; ○, calcite.
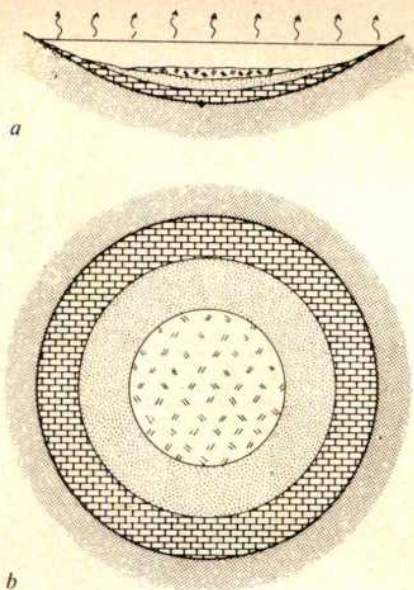
Fig. 7 Idealized bull's eye pattern of evaporite distribution typical of isolated basins. a, Cross-section; b, map.
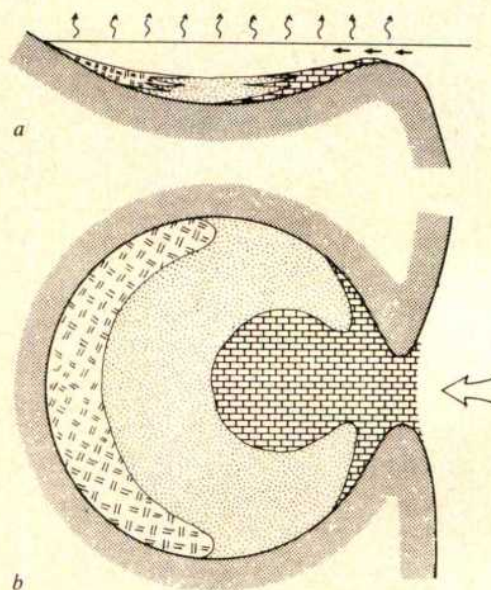
Fig. 8 Idealized tear drop pattern of evaporite distribution typical of partially restricted basins. a, Cross-section; b, map.

Finally, the distribution pattern of the Mediterranean evaporites is not at all what has been predicted on the basis of a deep water model; deep water evaporites should have a tear drop pattern rather than the bull's eye pattern typical of playa deposits. The latter is well known: a gradual desiccation of a playa should result in concentric zones of saline minerals[18,19], the outermost carbonate being the first salt to precipitate from a brine, and the inner core a most soluble salt (Fig. 7). By contrast, a restricted deep marine basin with an opening at one end would have less soluble salt deposited proximal to the opening and more soluble near the distal end (Fig. 8). If the
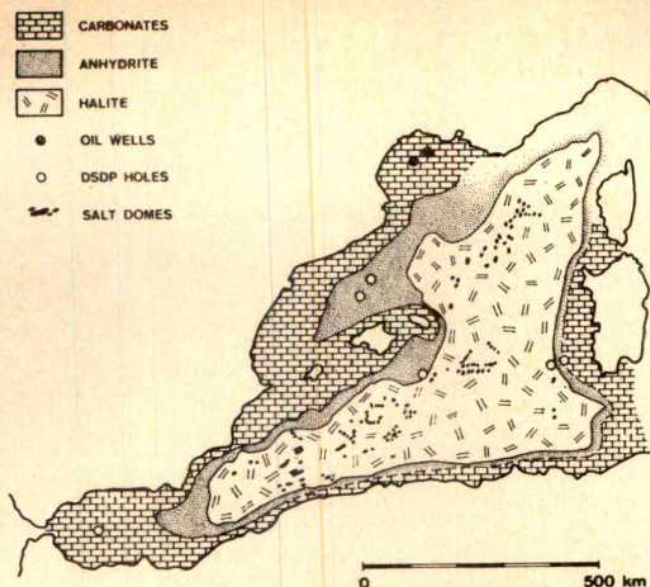
Fig. 9 Probable distribution of evaporites in the western Mediterranean Balearic Basin.

deep water model were applicable, we should have found potash salts and halite in the eastern Mediterranean, but only gypsum and/or dolomite in the western basins. The drilling results showed no evidence of such a "tear drop" pattern. In fact, drilling confirmed the suggestions arising from seismic profiling, namely that halite lies only in the deepest part of each Mediterranean basin and that the evaporite distribution conforms to a bull's eye pattern (see Fig. 9).

Geomorphological Evidence

A desiccated Mediterranean during the Late Miocene dictates that the base level of erosion must then have been thousands of metres below the sea levels. Shelf seas should have withdrawn from continental areas, and coastal plains and newly exposed shelf should have been dissected by rejuvenated streams. They should have cut canyons of steep gradients hundreds of metres into a slightly older marine sediment, and should have left alluvial and terrestrial clastics in the channels. Such a stream system should have been drowned during the final submergence of the desiccated Mediterranean in the earliest Pliocene.

Such an important regression has indeed been deciphered from the available geological records on land. In southern France, for example, a marine sequence, ranging up to Upper Miocene Tortonian, has been cut by a deep channel system. The channels were filled with alluvial gravels, which in turn underlie marine Pliocene sediments. The event recorded by the channel cutting has been known to stratigraphers as the Pontian regression, but its cause was unknown until we formulated our model of Late Miocene desiccation.

Pontian regression has also been reported in Egypt, where the River Nile at Aswan cut a gorge 200 m below sea level. It should be recalled that Aswan is a long way upstream, some 1,250 km from the coast; buried beneath the Marine Pliocene and Quaternary alluvial sediments of the Nile Delta area is a grand canyon comparable to the Grand Canyon of Colorado[11]. Similar buried gorges have been found in Libya, Syria, Israel, and other Mediterranean lands.

We might extend our reasoning a step further. When the Mediterranean was desiccated, the river channels should not only have cut the shelf margins, but should also have continued down towards the flat bottom of the Late Miocene playas, and extended 2,000 to 3,000 m below the present sea level. Post-Miocene sedimentation probably did not fill these channels completely, so drowned river valleys of Late Miocene age should be present on modern continental margins as submarine canyons.

Such submarine canyons have indeed been found, indenting the continental margins of southern France, Italy, Corsica, Sardinia and North Africa[8,22,23]. They were sculptured by streams and subsequently drowned during the Early Pliocene marine transgression. Similar submarine canyons are also present in the eastern Mediterranean[8].

The extension of Miocene streams down to the continental rises left behind floodplain silts and channel gravels. Such terrestrial clastics have been cored in a hole (site 133) at the foot of the continental rise to the west of Sardinia[5], and similar detrital deposits are present on the periphery of the Messinian evaporite basins of Sicily[24]. These occurrences are only explicable in terms of the model of basin desiccation.

History of Evaporite Deposition

The Mediterranean Sea, excluding the Black Sea, has an area of 2.5 million km^2 and a water volume of 3.7 million km^3. The annual loss by evaporation is 4.7×10^3 km^3. The annual precipitation is 1.2×10^3 km^3 and the annual volume delivered by river influx is 0.2×10^3 km^3. The net loss is thus 3.3×10^3 km^3 yr^{-1}. If the Strait of Gibraltar were closed today, the present Mediterranean could be evaporated dry in about 1,000 yr.

The thickness of halite salt that could be precipitated isochemically from one basinful of Mediterranean waters (averaging 1,500 m in depth) is, however, only about 20 m. Even if all the salt was deposited within a restricted basinal area covering one-third of the total, the resulting deposit should still be only 60 m thick. Yet the seismic record shows that the halite deposit under the Mediterranean may be two or three kilometres thick[5]. It is unlikely the freshwater influx from the rivers supplied all the salts, so repeated marine invasions must be postulated. Both the drilling results and the study of the correlative salt deposit of Sicily indicated that this was indeed the case; the Mediterranean was dried up and refilled repeatedly during the few million years represented by the Messinian stage. It should be recalled that the refilling of a basin could not have been instantaneous. Considering the inevitable evaporative losses during the transient stage, several basinfuls of water must have found their way across before the basin was filled up; thus each marine incursion into the Mediterranean might have brought enough salt to deposit a few hundred metres of halite in basinal areas. A detailed computation of the material balance budget led us to conclude that eight or ten marine invasions, represented by the interbeds of marine marls in the Upper Miocene evaporite-formation of Sicily, could have been sufficient to account for all the salts under the Mediterranean abyssal plains[5].

Although the flood gate at the Strait of Gibraltar apparently swung open and shut repeatedly during the Late Miocene, the gate was irreparably crushed at the beginning of the Pliocene. The earliest Pliocene sediment of the Mediterranean is a deep marine ooze, characterized by a cold water bottom fauna. Although the recurrent Messinian "refills" might have been related to spill-overs caused by eustatic rise of the world wide sea level, the final deluge was probably related to a rifting movement along the Azores–Gibraltar fracture zone. The initial gap was deep enough to permit the entrance of deep Atlantic bottom faunas into the Mediterranean. The Strait of Gibraltar was gradually shoaled during the Pliocene, and eventually the supply of deep Atlantic waters was cut off, causing the extinction of the cold Mediterranean benthonic faunas. Yet the Strait is still open sufficiently to permit the reflux of partially evaporated Mediterranean waters so as to keep its salinity only slightly above that of the open ocean.

Explaining an Improbable Fact

We have presented in this article the evidence which led us to conclude that the Mediterranean was a desiccated deep basin some 6 million years ago. The full documentation of the data will be published in our cruise report[5]. We realize that our

deduction seems improbable because none of the desert basins today are comparable in size or depth to a desiccated Mediterranean. Yet the improbable fact that the Mediterranean Sea is underlain by a salt deposit demands an improbable explanation. We welcome comments from our colleagues in the Earth and biological sciences, particularly if some of their own observations bear out, or disprove, the idea that the Mediterranean was a desert during the Late Miocene.

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Voltage Dependent Charge Movement in Skeletal Muscle: a Possible Step in Excitation-Contraction Coupling

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It is suggested that a link in excitation-contraction coupling involves the movement of a fixed amount of charge free to move between different locations across the membrane.

STARTING with the experiments of Huxley and Taylor[1] and Huxley and Straub[2] the view has developed that, under physiological conditions, contraction in skeletal muscle is triggered by depolarization of the membranes of the transverse tubular system (T-system)[3]. This network of tubules extends throughout the cross-section of a fibre[4] and is positioned at regular intervals along the fibre length[5], thus providing a means whereby a change in surface potential can be rapidly transmitted into the interior[6,7]. There is also evidence[8-10] indicating that the final stage of excitation–contraction coupling involves a release of calcium ions into the myoplasm from its intracellular storage location, the sarcoplasmic reticulum (SR); the elevated Ca^{2+} then activates the contractile proteins[11]. It has not been clear, however, how a change in potential across the tubule membrane could bring about the release of Ca^{2+} from the neighbouring SR. The experiments reported here are an attempt to detect an ionic current or movement of

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charge across the T-system membrane which could play a role in triggering this response.

Voltage-clamp Measurements

In our experiments sartorius muscles from English frogs, *Rana temporaria*, were cooled to approximately 2° C in a solution designed to eliminate virtually all of the time and voltage dependent changes in sodium and potassium currents. The composition was 117.5 mM tetraethylammonium (TEA) chloride, 5 mM RbCl, 1.8 mM $CaCl_2$, tetrodotoxin (10^{-6} g ml.$^{-1}$), and 1 mM Tris-maleate buffer to give a pH of 7.1. Movement due to contraction was practically eliminated by making the solution hypertonic with sucrose addition, 350 to 583 mmol to 1 l. Sucrose hypertonicity appears to have little effect on calcium release as the heat of activation is decreased only 10 to 20% on adding 450 mmol sucrose per 1 normal Ringer's solution[12]. Voltage-clamp measurements were carried out using the three microelectrode technique described by Adrian, Chandler and Hodgkin[13]. In this method two voltage sensing microelectrodes were positioned at intervals 1 and 21 from the end of a particular fibre and a third electrode was used for passing current, as is shown in Fig. 1A. The membrane current density at x=1 is related to the difference in potential $\Delta V (= V_2 - V_1)$ by the relation

$$i_m = 2\Delta V/3r_1 l^2 \tag{1}$$

in which i_m is current and r_1 is internal resistance per unit length of fibre. Feedback electronics were used to set the

potential V_1 at a command level E_c. The voltages V_1 and ΔV were displayed on a 'Tektronix 565' oscilloscope and photographed; in addition, one of the signals, usually ΔV, was integrated successively over intervals of 1–2.5 ms with a 'Technical Measurement Corporation Computer of Average Transients', Model 1000, or sampled at 0.5 to 2.5 ms intervals using a 'Fabritek Signal Averager', Model 1072, with a 20 µs filter in the input circuit.

Fig. 1B shows two sets of photographed records of V_1 (upper trace) and ΔV (lower trace). In each case a depolarizing voltage pulse of 41 mV was applied to the fibre; in the upper records (a) the pulse was superimposed on the holding potential, -79 mV, and will be denoted (-79 mV, 41 mV), whereas in (b) a conditioning step was applied 100 ms before the start of the pulse so that the 41 mV pulse was superimposed on a potential of -126 mV (-126 mV, 41 mV), Both ΔV records show an initial 2 to 3 ms surge, corresponding to the capacitive transient, followed by a relatively flat trace. Although the two sets of records look very similar, small differences are seen on closer examination. This is shown most clearly by taking the difference between the two records; Fig. 1C, trace c, shows the result of summing the difference four times. It is apparent that the 41 mV step from -79 mV produced a small, outward current over and above that seen with a step from -126 mV. The extra component decayed with time to a steady level which corresponds to a slight nonlinearity in the current-voltage curve.
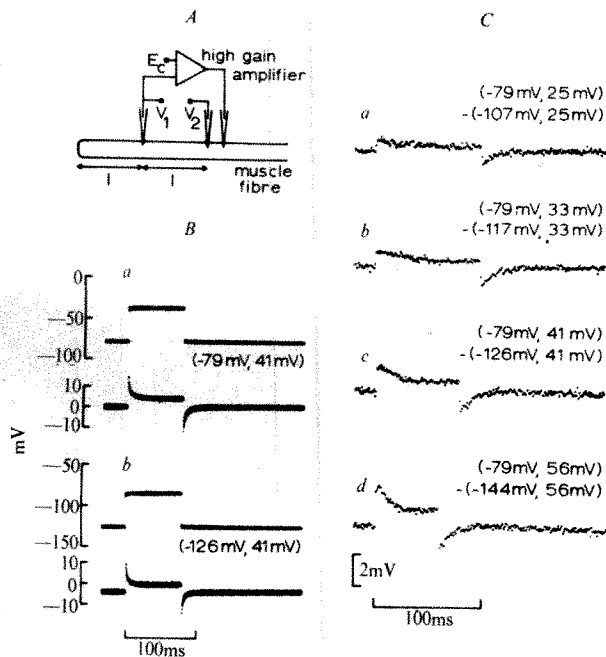
Fig. 1 A, Diagram of the three microelectrode technique. B, Single traces of V_1 and ΔV from fibre 113.2, holding potential= -79 mV, l=172 µm: a, pulse applied from holding potential; b, potential stepped to -126 mV 100 ms before start of pulse. C, Photographs of Fabritek display, fibre 113.2. Each trace represents the difference in ΔV between records such as Ba and Bb, summed four times to improve signal-to-noise. The vertical calibration refers to a single difference. The sampling rate was 1 kHz.

Two other features shown by the four records in Fig. 1C are of interest. First, the magnitude of the extra outward current increased as the voltage pulse was increased. Second, on repolarization there was a tail of inward current, and the area above the tail was approximately equal to the area under the transient part of the extra outward current, as indicated in Fig. 3A.

As a quantitative relationship of the type shown in Fig. 3A

has strong implications about the nature of the extra charge movement, the effect of pulse duration on the "on" and "off" areas was studied. One such experiment is illustrated in Fig. 2. Signal averaged records of (-80 mV, 47 mV) minus (-127 mV, 47 mV) for 10, 20, 40 and 80 ms pulses are shown in Fig. 2A. It is clear that the amplitude of the tail was small for short pulses and that it tended to reach a steady level as the duration was increased. In all cases, the area of the "off" response seems to match the area of the "on" (Fig. 2B).
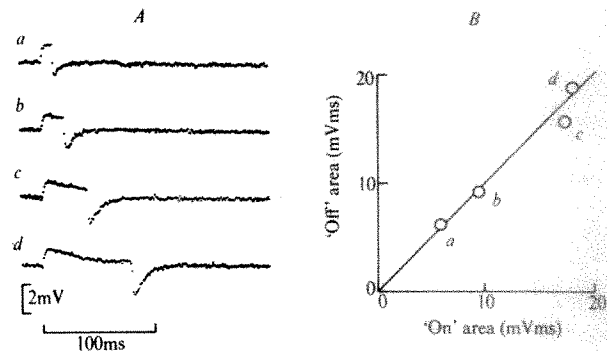
Fig. 2 Effect of pulse duration on charge movement. A, Photographs of Fabritek display, fibre 111.1, holding potential -80 mV, l=205 µm. Each trace shows the difference (-80 mV, 47 mV) minus (-127 mV, 47 mV) signal-averaged four times, 1 kHz sampling rate. Pulse duration: a, 10 ms; b, 20 ms; c, 40 ms; d, 80 ms. B, Comparison of "off" areas with "on" areas, from part A. The 45 degree line represents perfect agreement. The final level in trace d was subtracted from all records in calculating the "on" area.

That the results fit the relation (area of "off")=(area of "on") suggests that the transient extra current is due to the displacement of a quantity of charge trapped in or near the membrane. It might also be possible, however, that the agreement of areas is fortuitous and that the current is due to a change in membrane conductance, for example, to calcium. The current seen with the step depolarization would then be the sum of a constant outward current and a slowly developing inward calcium current. Although several arguments oppose this view, the most direct is based on the type of experiment in Fig. 2A. The "on" current 10 ms after the start of the pulse shows little or no decline and, presumably, the lack of development of the hypothetical inward current. The peak tail current following a 10 ms pulse (2Aa), however, is already one-third maximum as determined in 2Ad. This lack of correspondence as well as the agreement of areas in Figs. 2B and 3A argues against a conductance change and in favour of a charge displacement for the underlying mechanism.

Relationship between Charge and Membrane Potential

The next question is whether there is a simple relationship between the amount of charge which moves and membrane potential, V. Other experiments, not given here, show that little if any extra charge movement occurs for changes in potential in the range V less than about -100 mV. Defining $A(V)$ as the area of the extra transient (which is proportional to charge) we may set $A(V)=0$ for $V < -100$ mV. The relatively small value of $A(-79$ mV) can then be estimated by comparing areas for pulses from -98 mV and -79 mV, represented by the squares in Fig. 3A; this value for $A(-79$ mV) is shown in Fig. 3B and was used to adjust the other points in the figure. The theoretical curve was drawn according to the expression

$$A(V)/A_{max} = [1 + \exp - (V - V')/k]^{-1} \qquad (2)$$

with $V' = -53$ mV, $k=8$ mV and $A_{max}=22$ mV ms. Equation (2) is the same functional form used by Hodgkin and Huxley

to describe steady-state inactivation of the sodium conductance in squid axons[14]. Results from this and four additional experiments gave an average value of -49 mV for V', 11 mV for k. Experiments in isotonic solutions below the contraction threshold gave values for k similar to those observed here, but depolarization was insufficient to determine V'.
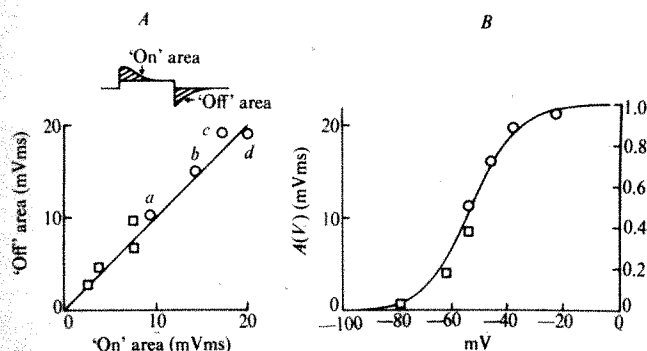
Fig. 3 Effect of membrane voltage on charge movement. A, Comparison of "off" areas with "on" areas. ○, Measured from the experiment in Fig. 1C; □, measured from a similar set of traces taken somewhat earlier from the same fibre. The purpose of this run was to compare depolarizations to -62 and -54 mV from two conditioning levels -79 and -98 mV. The 45 degree line represents "on" area = "off" area. B, $A(V)$ versus V. The symbols ○ and □ represent the average areas from the same symbols in part A, adjusted for the small but finite value of $A(V)$ around the holding potential. The scale on the right is normalized to range from 0 to 1 and serves as the ordinate for the calculated curve.

Our results are clearly consistent with a model in which there is a fixed amount of charge free to move between different locations across the membrane or between locations which see different proportions of the total membrane potential. (A mathematically indistinguishable model can be based on rotation of permanent dipoles.) In the simplest case one might imagine just two positions, 1 and 2, which see a difference in voltage αV proportional to the total membrane potential. When the voltage is very negative, all the charged groups would be in position 1; with depolarization some of the groups would move to position 2; on repolarization the groups that moved to 2 would return to 1. These movements of charge would produce transient currents resembling those observed in the present experiments.

The model can be made quantitative in the following way. If f_1 is the probability of the group being in position 1, f_2 in position 2, the Boltzmann expression gives

$$f_1/f_2 \propto \exp[-\alpha z FV/RT]$$
$$= \exp[-\alpha z F(V - V')/RT] \quad (3)$$

where z is the valence of the particle, V' is the potential at which $f_1 = f_2$, and F, R, and T have their usual meaning. As $f_1 + f_2 = 1$, equation (3) can be solved for f_2 to give the expression in equation (2) where $k = RT/\alpha z F$. The value of 8 mV for k in Fig. 3B corresponds to $|\alpha z| = 3.0$; the average value of 11 mV gives $|\alpha z| = 2.2$. Thus, if α were close to unity, the charged group would have a valence of magnitude two to three.

Properties of the Charge Movement

Although the physiological role of this charge movement is unknown, it is interesting to note that it has certain properties which could make it useful as a trigger mechanism. First, the range of membrane potentials in which the charge movement occurs is the range in which many of the electrical and mechanical properties of muscle are strongly regulated. Second, the currents produced by the charge movements are sufficiently small that they would not interfere with the normal propagation of an action potential. Third, the movement of charged groups from a resting position to a new location on depolar-

ization, and the return on repolarization, could involve a physical motion of some tens of Angström units, a motion which could correspond to turning a molecular trigger on and off.

The charge movements described here may in many ways be qualitatively similar to "gating" currents in squid axons, recently found by Armstrong and Bezanilla[15], which may play a role in activating sodium channels. Quantitative differences, however, are clear; in muscle the amount of charge per cm^2 of total membrane (surface+T-system) is roughly three times that in squid axon and the time course is twenty to one hundred times slower. This makes it improbable that the charge movements in muscle would be linked to gating sodium channels.

A more likely speculation which can serve as a guide in planning future experiments would be to suppose that the charged groups were located in the membranes of the T-system and that their displacement constituted a step in excitation–contraction coupling. If the groups were attached to long molecules which extended to the adjacent projections of the SR terminal cysterna membrane[16], they would provide a means by which the potential across the wall of the T-system could be sensed by the SR; in fact, movement of the molecules could directly regulate the release of Ca^{2+}. In the simplest form one might imagine that the rate of Ca^{2+} release could be proportional to $A(V)$ (see Fig. 3B) or some function of $A(V)$. The threshold for contraction, -50 to -55 mV in normal Ringer[7] and possibly more negative in the solutions used here (see refs. 17, 18), would be the potential at which the rate of release was just greater than the rate of uptake. Along these lines it is of interest to estimate the number of charged groups per cm^2 of muscle membrane. In the experiment in Fig. 3 the electrical capacitance was measured according to the method of Adrian et al.[13]. Using a value of 1 μF per cm^2 of membrane[19,20], the values of A_{max} and k in Fig. 3B give 300 charged groups per μ^2 of membrane (surface+T-system). This number is roughly similar to the number of electron dense "feet" joining the T-tubule and the periodic projections of the SR membrane; these occur with a frequency of 700 per μ^2 of tubule membrane[21]. Thus, it would be numerically possible for approximately one charged group to be associated with each "foot".

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African Infant Precocity and Some Social Influences during the First Year

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In African infants precocious in both mental and motor test performance during the first year of life, environmental factors contributed at least 25% to test score variance. Even in the first year, therefore, social factors must be considered in evaluation of psychological development of these infants.

SEVERAL studies[1-3] have led to the widely-held belief that sub-Saharan African infants are precocious in their psychological development. These studies leave much to be desired methodologically[4]. Nevertheless, the preponderance of evidence suggests that compared with infants of the United States, of England, and of France, African infants during their first year of life are precocious in motor (neuromuscular) development, and possibly in mental (perceptual-sensory) development as well.

This precocity seems to be less marked for infants from westernized and/or middle class family backgrounds than for those from traditional and/or lower class families[5-7]. These observations imply that the precocity in sub-Saharan African infants, which might be thought to be genetically based[7], may also be substantially influenced by social factors.

The purpose of this study, therefore, is (1) to investigate whether or not there is development precocity, using more reliable individual measures based on longitudinal study of the infants, and (2) to assess the relationship between selected social and demographic variables and psychological development.

The sample comprised sixty-five infants born between July 1 and December 31, 1969, residing in a periurban Kikuyu, predominantly agricultural community of 4,500 people, approximately 25 miles from Nairobi. An estimated total of 100 infants was born during this period and ninety of their mothers agreed to participate in the study. Seven infants were lost to the study because their families moved from the community or for some other reason their data are incomplete. Eighteen infants served as controls for another segment of this study and were not tested longitudinally. Of the sixty-five sample infants, thirty-four were male and thirty-one female. Twelve were first-born; among the others, the median number of older siblings was

five, including eleven subjects in the sample having eight or more older siblings.

The Bayley Test[8] in standard form was used for all infant testing. The items used in this test divide into two scales, mental (perceptual-sensory function) and motor (neuromuscular function). Testing was done by a British-trained Kenyan nurse who was bilingual (Kikuyu, English) and whose family lived near the village. Ten non-study infants were used in the training procedure. Interobserver item agreement on the test for the final two pretest infants reached 85%.

Each infant was tested at approximately 2-month intervals, beginning in January 1970, on at least four and at most eight occasions. Testing was done in the morning or in the afternoon at times when the infant was judged alert and cooperative. All infants were breast-fed during the entire period, the older infants receiving supplementary food. Evidence of gross malnutrition was absent on two clinical examinations provided at the beginning and end of the study.

Demographic and social information was obtained from interviews of the mothers conducted by two college-level Kikuyu-speaking young women. In addition to routine demographic information, data were collected on family structure, educational achievement, economic status and density of the household. A check list was used to obtain a brief description of the material amenities available within the household.

Within this rapidly changing community, there was noticeable variation in the social and economic circumstances of the families for such variables as the amount of land available to each family, the educational level of the parents, the maintenance of traditional practices (for example, the practice of polygamy) and the contact with the urban environment of Nairobi.

Test results were first analysed by comparing the performance of Kikuyu infants on individual test items against United States standards[8]. For each item, the number of infants able to perform the task described by the test item earlier than the United States median age for performance of that task, and the number unable to perform the task at the United States median age, were tabulated. Kikuyu infants surpassed United States performance on thirty-eight items for the mental test and twenty items on the motor test; they lagged behind United States performance for seven items in the mental test and two items on the motor test. There was no apparent pattern in the type of items which differentiated the two groups, though our impression

is that Kikuyu infants lagged behind the United States performance on items involving implements which were less familiar in their environment than in the United States.

These findings suggest that if Kikuyu infants were scored by United States standards using items passed at a given age, they would tend to show performance superior to United States expectations . Each infant was given a developmental quotient (DQ) for the mental and motor tests using United States conversion tables[8] at each of his first four test sessions. The four DQs were averaged to get a single score for each infant on the mental and motor tests. The mean mental score for sixty-five Kikuyu infants was 108.4 (s.d.=24.4) ; the mean motor score was 129.5 (s.d.=38.9). The expected United States average score would be 100.0, with expected standard deviation ranging from 16 (if test-retest reliability is 100%) to 8 (if test-retest reliability is 0%). The variabilities of the Kenya sample are somewhat but not significantly larger than that expected in a United States sample. On both the mental and motor tests, Kikuyu youngsters score significantly better (t test, P<0.01) than would be expected in a United States group.

The precocity on the motor test corroborates the findings of Geber and is quite similar to the Uganda findings of Kilbride[9] obtained using the Bayley Test in a cross-sectional sample. The finding of precocity on the mental test, though not unanticipated, was surprisingly clear, and consistent with reports for African infants and United States black infants[10,11]. The Kikuyu infants performed better than the United States black group on the mental test, as well as on the motor test. This finding may be attributable to the fact that in this study testing was done by a bilingual, bicultural tester, from the same ethnic group as the infant. This may be important in infant testing, especially for infants between the ages of 6 and 12 months, because fear of the stranger is likely in this period of development. It should also be noted, however, that maternal caretaking within the Kikuyu community involves more physical contact with the infant in the first 6 months of life, and therefore might also account for those differences (additional data on maternal behaviour will be presented elsewhere).

Fig. 2 Comparison of motor test performance (Bayley) for Kikuyu (●), UK white (○), US black (▲), and US white (△) infants during the first year.

deviation. It is obvious that·the Kikuyu mental and motor scores exceed combined United States white and black[11] and United Kingdom white[12] scores at all points during the first 12 months of life.

We used a polynomial regression and a repeated measures design[13] to examine the relationship between test performance and selected social and demographic variables. A Kenya-Kikuyu curve was computed for both mental and motor scores and a test score for each infant was calculated relative to that curve. For convenience, these scores were standardized to a mean of 100 and a standard deviation of 16.

These scores were then used as the dependent variables in a step-wise multiple regression analysis[13] using as independent variables thirty-three selected social and demographic variables including such items as sex, birth order, age, education of parents, an evaluation of the modern attitudes of the mother, degree of contact with the urban environment of Nairobi, family structure, modern amenities available within the household, economic status of the family, and the household density within different age groups.

Fig. 1 Comparison of mental test performance (Bayley) for Kikuyu (●), UK white (○), US black (▲), and US white (△) infants during the first year.

Another way to present these data is shown in Figs. 1 and 2. The grand total of 376 test sessions (sixty-five infants, four to eight sessions per infant) was subdivided by the age of the infant to the nearest month at the time of testing. Mean scores were calculated for each month. Fig. 1 presents the mean number of items passed at each age for the mental test, and in Fig. 2 for the motor test. The vertical line represents a positive and negative deviation of one standard

Table 1 Multiple Regression Analysis of Bayley Test Scores with Demographic Factors

(N=65)			
Mental		Motor	
Multiple correlation coefficient= +0.51		Multiple correlation coefficient= +0.45	
	Correlation factor vs test		Correlation factor vs test
Economic	+0.37 *	Number of individuals aged > 40	+0.30 *
Modern amenities	+0.36 *	Economic	+0.26
Number of household members aged 21–40	−0.22	Number of household members < 3 yr	−0.23
Number of household members aged 13–20	+0.20	Sex of infant ♀>♂	+0.17

* P<0.05.

The results are shown in Table 1. The four indicated variables contributed the largest share to multiple correlation coefficient (+0.51) for the mental test score. Two of these variables, economic status and modern amenities available, yield individual correlation coefficients of 0.37 and 0.36 with mental test score, each significant at the 5% level. Infants in families with greater economic resources and with more modern amenities such as calendars, clocks, books, and so on, performed better on the mental test.

The same type of analysis for motor test score indicates that four of the variables made the largest contribution to the multiple correlation coefficient of +0.45. The only significant positive correlation, between the number of indi-

viduals in the household past age 40 and motor ability, suggests that additional caretaking of the infant by an older woman or grandmother contributed to infant motor development.

Further corroboration of the relationship between the test scores and social and demographic variables is shown in Tables 2 and 3. Those infants born to fathers of higher income, more training, and education score higher on the mental test than do infants born of fathers with less income, training, and education. Similarly, for the motor scores, those infants with fathers in the upper economic range score higher than other infants. In the case of the density of the household, those infants where there are two or more individuals aged 41 to 60 score the highest, whereas those without such individuals score the lowest.

Table 2 Relationship of Mental Test Scores (Kenya Norms) to Selected Social Factors

Father's education	N	Kenya DQ
Standard 7–8, Form 1–11	30	105.6
No information	10	100.5
No education	10	97.8
Standard 1–6	15	89.9
Cash income		
Yes	34	102.1
No	24	89.3
No information	7	104.4
Father's occupation		
Farmer, >2 acres	6	106.0
Position requiring training	29	104.6
Position requiring no training	11	92.5
Farmer, <2 acres	8	85.3
No information	11	107.4

The body of results for both mental and motor tests does not support the observations of Geber[6] suggesting that infant precocity is negatively related to social class, and to the observations of Bayley[11] which indicate that there is no relationship between performance and social class. While it is difficult to reconcile the results of this study with the findings of these other studies, the differences found between this study and other studies may be due to sampling procedure and testing methodology. Our sample consisted of approximately 90% of the available infant population and was drawn from the general community and not from a hospital or clinic population. Our testing was repeated several times on the same infant during the infant's first year, in contrast to cross-sectional methods employed in these other studies.

Table 3 Relationship of Motor Test Scores (Kenya Norms) to Selected Social Factors

Presence of individuals >41	N	Kenya DQ
Two	15	106.9
One	17	103.7
None	28	95.2
No information	5	93.1
Cash income		
Yes	34	102.7
No	24	89.5
No information	12	100.4

A definitive explanation of why sub-Saharan African infants have precocious mental and motor development during their first year of life, and why their test performance is apparently influenced by the economic level of their families and other social factors, cannot yet be given. From what is known about traditional Kikuyu marriage customs[14-16], it is possible that the bride-wealth system has produced assortive mating on the basis of social and economic status. This assortive mating over many generations could lead to the developmental differences observed, even in the relatively restricted range of social and economic differences observed currently within this community. Regardless of the selection pressures that may have been operative in the past, however, we have found that contemporary social and economic conditions are positively related to the infant's psychological development in the first year.

This is particularly interesting if the observations of Parkin and Warren[17] are correct. They found very few significant differences between African infants of high income families, African infants of low income families, and European infants of middle class background born in Kampala, when examined in the first five days of life, using a modified Prechtl[18] examination procedure. None of the differences reported favoured one group over the other. Assuming that Kikuyu infants are similarly non-precocious at birth, then our findings of precocity developing during the first year, while conceivably genetically determined, lend support to theories emphasizing environmental influences on infant development during the first year of life.

Another possible environmental influence is nutrition, but there was no evidence for gross malnutrition among the infants, and no infants were lost to the study because of illness or death. Whether malnutrition of mothers, related to the economic level of the family, caused intrauterine deprivation of some infants, is not known. But in any case malnutrition would be expected to diminish the performance of the Kikuyu babies.

In agreement with others[19], we recognize that genetic factors account for a large proportion of the variability of mental and motor test performance especially in the infant's first year. The remaining variance (approximately 25%), however, is not random, but can be associated with identifiable social and demographic variables predictive of precocious psychological development.

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LETTERS TO NATURE

PHYSICAL SCIENCES

Radio Emission from the Close Binary b Persei

WE report the detection of faint intermittent radio emission from the close binary star b Persei. Concurrent observations at 2,695 and 8,085 MHz were made with the NRAO interferometer on spacings of 900, 1,800 and 2,700 m. The total observing time was 14.4 h, mostly in short periods between February 7 and February 15, 1972. Further brief observations were obtained on April 28 and June 21, 1972.

Radiation from the direction of b Persei was seen during about 5 h. The position of the intermittent radio source coincides closely with the position given in the SAO catalogue for b Persei:

$$\alpha_{1950} = 04 \text{ h } 14 \text{ min } 28.5 \text{ s} \pm 0.13 \text{ s}, \ \delta_{1950} = +50° \ 10' \ 28'' \pm 2''$$
(Radio)

$$\alpha_{1950} = 04 \text{ h } 14 \text{ min } 28.443 \text{ s}, \ \delta_{1950} = +50° \ 10' \ 28.94''$$
(Optical)

The very close positional agreement and the intermittent nature of the radio emission are convincing evidence that b Persei is a radio star.

The source was seen at 8,085 MHz for a few hours on February 7–8 and February 11–12, at an average flux density of 0.012 ± 0.004 f.u. There may have been radiation at 2,695 MHz during the event of February 7–8, with a flux density of 0.005 ± 0.003 f.u., but the detection is by no means certain. At all other times, the flux density was less than 0.008 f.u. at both frequencies. The temporal structure of the radio emission is well shown by the observations made during the event of February 11–12. No radiation was seen from 1914 UT until 2214 UT (February 11). From 2214 UT until 0246 UT (February 12), radiation at an average level of 0.012 f.u. was seen at 8,085 MHz. No radiation was seen during the 2 h following 0246 UT. During this entire time (about 10 h), the b Persei field was observed intermittently at intervals of 25 min out of each hour.

Clearly, the source flared to an observable intensity for about 5 h on at least two occasions. The data are still sparse, but they suggest that the b Persei radio emission is not unlike that of Algol (β Persei)[1-4], although it is much fainter. The essential points of similarity are the flare-like variability of the radiation, and its greater strength toward shorter wavelengths.

The close binary b Persei joins β Persei[1-4], β Lyrae[1,2] and α Scorpii B[5,6] in the class of binary systems with flaring radio emission, but without known X-ray emission. It is an ellipsoidal variable with a period of 1.52738 day; its light curve has an amplitude of 0.06 mag at visual wavelengths[7]. Heard[8] has confirmed earlier work indicating that the orbital elements of the system are probably changing with time. As in the case of β Persei, it is tempting to suspect that the radio emission is related in some way to binary mass exchange phenomena.

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The Missing Planet

THE idea that the asteroids are fragments of an exploded planet was first put forward by Olbers more than 150 yr ago and has since been widely accepted. Recently Ovenden[1], in an attempt to account for Bode's Law, has argued persuasively that a planet of 90 $M_\oplus$ vanished between Mars and Jupiter some 16 m.y. ago. According to this point of view the asteroids are remnants of this event.

Other possibilities have been suggested, however, for the origin of the asteroids. For example, Kuiper[2] suggested that they are remnants of successive collisions which occurred between a few primaeval planetoids; Alfvén[3] and others regard the asteroids as being in the process of forming a single planet by accretion. The difficulty of disrupting a planet of 90 $M_\oplus$ was mentioned by Ovenden. Here we eliminate mechanisms which are incapable of providing the energy needed both to break up the hypothetical planet and to remove most of its mass beyond the Solar System. The mechanisms for disrupting a planet might be chemical, gravitational or nuclear in nature.

In the chemical case, to dissipate a planet of mass M and radius R, an energy $E \sim GM^2/R$ is required, where G represents the gravitational constant. For a mean density comparable to that of the Earth, $R \sim 4.5 \ R_\oplus$ and $E \sim 8 \times 10^{42}$ erg, or $\sim 1.5 \times 10^{13}$ erg g^{-1}. This seems to exclude the possibility of a chemical mechanism: the detonation energy of TNT, for example, is $\sim 5 \times 10^{10}$ erg g^{-1}.

Gravitational tidal forces due to the Sun or Jupiter are negligible at a heliocentric distance of 2.5 a.u. The missing planet might conceivably have strayed within the Roche limit of Jupiter. Such a close passage would greatly disturb, if not disrupt, the Galilean satellite system, which, according to Ovenden's theory, required 2×10^9 yr to settle into the observed resonances. Consequently the missing planet could not have strayed so close a mere 1.6×10^7 yr ago.

Nuclear effects might be the heat released by radioactive decay somehow converted to kinetic energy, fusion, or a chain reaction. Radioactive decay is a slow process and if an explosion is to result the energy generated must be stored. Thus a high pressure core must develop, constrained by a solid mantle until bursting occurs. The crushing strength of rock is $\sim 10^9$ erg g^{-1}, so even if the entire planetary mass were involved in containing the central force, breaking point would be reached long before the required 1.5×10^{13} erg g^{-1} was available. Consequently any explosion would lack the energy required by a factor $\sim 10^4$.

A similar objection applies to the hydrogen fusion reactions with the exception of $^2D + {}^1H \rightarrow {}^3He + 5.5$ MeV which has a reaction time of only ~ 6 s. But this reaction is only significant at temperatures above 5.4×10^5 K and this is unattainable in planetary interiors. More generally, masses less than 2.4×10^4 $M_\oplus$ are too small to become hot enough for nuclear reactions.

Assuming a relative ^{235}U abundance throughout the planet equal to the terrestrial crustal abundance, there is just enough energy to disperse the planet if the ^{235}U could be assembled into a super-critical mass. In addition a chain reaction has the advantage that the necessary force could be developed in less than the travel time of shock waves through the planet. But it is clearly improbable that, in nature, enormous numbers of sub-critical masses of ^{235}U could be assembled and brought together simultaneously within the planet.

There remains the possibility, mentioned by Ovenden, that the 90 $M_\oplus$ might have been in the form of a ring. For the ring to dissipate, the particles must either leave the Solar System or be absorbed into the Sun.

In the first situation the energy difficulties are as severe as in the planetary case (1.9×10^{42} erg required) with the additional problem that a suitable mechanism for dispersal is even more difficult to conceive. In the second case the ring particles are required to lose virtually all their angular momentum over a very short time scale (say, $< 10^6$ yr). The only effective mechanism for systematic angular momentum loss is the Poynting-Robertson[4] effect. To be removed in 10^6 yr or less, the particles must have been < 0.02 cm in diameter; but for the ring to have persisted for the previous 4.5×10^9 yr, they must have been $\geqslant 600$ cm in diameter. No mechanism seems to exist whereby bodies of this size could exist for so long and yet suddenly disintegrate on a time scale $< 10^6$ yr.

We conclude that the destruction of a planet or ring in the recent past, with the mass required by Ovenden's theory, is physically improbable: one must look elsewhere for an explanation of Bode's Law and the existence of the asteroids.

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Martian Centre of Mass — Centre of Figure Offset

A DIFFERENTIATED crust and possible internal convection are suggested by this first report of a martian centre of mass-centre of figure offset. Martian topography from Earth based radar observations[1-3] has been reported for latitudes extending from about 22° N to about 16° S. These observations reveal a gross topography which is relatively insensitive to latitude and which shows variations in excess of 10 km (Fig. 1). Local topographic variations inferred from the Mariner ultraviolet spectrometer observations[4] are consistent with the radar data.
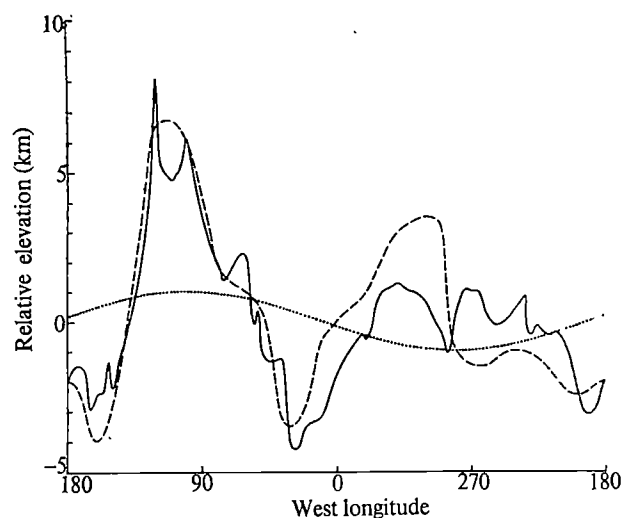
Fig. 1 Relative elevations of the martian surface at $\approx 15°$ S (—) and $\approx 11°$ N (- - -) as a function of west longitude[2,3]. The first harmonic of the more accurate topography at 15° S (. . .) is also shown. The amplitude and phase of this first harmonic determine the magnitude and orientation, respectively, of the centre of mass-centre of figure offset.

Because these topographic data, deduced with respect to the centre of gravity, are complete in longitude along latitude bands close to the equator, some estimate can be made of the magnitude and direction of the centre of mass-centre of figure offset of Mars. The most accurate topography is that reported[3] at about 15° S latitude. This has a surface resolution of 1.3° in latitude and 0.8° in longitude with a precision in surface height measurement approaching 75 m in regions of high radar reflectivity.

A Fourier analysis of these data reveals a first harmonic, corresponding to an offset of about 1 km, with the centre of figure displaced, with respect to the centre of mass, in the general direction of Tharsis (Fig. 1). The Tharsis region, a broad highland standing about 5 km above the mean equatorial relief, is the site of major volcanic features on Mars, including Nix Olympica and the three aligned volcanic features known as North, Middle and South Spots[5,6]. Near the location diametrically opposite to Tharsis is the Hellas basin, the largest circular basin on Mars (about 2,000 km diameter) with a depth[7,8] of at least 3 km.

The martian centre of mass-centre of figure offset strongly suggests[9] that the planet has a differentiated crust, lighter than the subcrustal material and thicker under the Tharsis highlands than under the region between Hellas and Syrtis Major. For a difference of less than 10% between the density of the crustal rock and the mean density of Mars, the difference in crustal thickness must be greater than 20 km.

Mars is not unique in possessing a centre of mass-centre of figure offset. Offsets of comparable magnitude are known for the Earth[10,11] and the Moon[9,12]. These offsets are clearly associated with the asymmetry of the terrestrial continent-ocean basin and lunar highland-mare distributions. There is a wealth of geologic, seismic and gravimetric evidence[13] that the terrestrial continental crust is lighter and thicker than the oceanic crust. As well as the lunar offset, there is additional evidence that the far side crust beneath the lunar highlands is lighter and thicker than the near side crust. This can be seen from the differences in chemical composition[14] between the highland and mare material and the absence of a significant positive gravity anomaly[15] in the front side highlands with respect to the maria, from which we may infer the thickness of crust beneath the highlands even on the far side.

Asymmetric crustal distributions are most likely produced by large scale internal convection during or after the period of crustal differentiation[16]. Convective motions of subcrustal material would lead to an accumulation of lighter crustal

material above regions of downwelling, making the crust thicker there and thinner in the region of upwelling. A less likely mechanism for producing asymmetric crustal distributions is the action of a few large impacts. Massive throwout of crustal material from an impact crater and subsequent partial filling of the crater with heavier subcrustal material could produce a centre of mass-centre of figure offset.

In the case of the Earth it is now generally accepted that some form of mantle convection is responsible for the present distribution of the continents. If, in the case of the Moon, the asymmetry were due to impacts, the thinnest crust should be found in the region of the largest impact features. This, however, does not seem to be the case. The largest front side impacts, Imbrium and Orientale, lie roughly 60° and 130°, respectively, from the location of the thinnest crust at about 35° east longitude, as implied by the observed[9] offset. The recent discovery[12] of an unfilled, Imbrium-sized basin on the lunar farside further implies that early large impacts on the Moon occurred with no less frequency on the far side, making it highly unlikely that they produced the observed asymmetry in lunar crustal distribution. Thus past internal convection seems[9] to be responsible for the lunar offset.

The occurrence of the large martian volcanoes in the Tharsis region strongly favours an internal convective origin for the asymmetric crustal distribution and resultant offset. Thus we expect that the Tharsis region is the site of downwelling convective motions with the ensuing accumulation of a relatively thick, light crust. The associated volcanism could then result from frictional heating along local fracture zones stressed by the downward motion. The morphology[6] and partial alignment of the martian volcanoes in the Tharsis region is qualitatively similar to that of the composite, or strato, volcanoes associated with downwelling regions on Earth, although the analogy is crude at best. We note that the morphology of the martian volcanoes is inconsistent with the massive flooding that would be expected in a region of upwelling. The Mariner 9 imagery[5,6] also revealed other evidence of extensive volcanic and tectonic modifications of the martian surface which might reflect deep internal processes. The location of the Hellas basin near the direction of the thinnest crust, as implied by the offset, might suggest that an impact produced the asymmetric crustal distribution. But such an impact alone could not account for the volcanism at Tharsis, although it could have influenced a pattern of internal convection. That the latter might be the case may be indicated by the nearly diametrically opposite positions of the Tharsis volcanic region and the Hellas basin.

The magnitude of the low order components of the martian gravity field[17] and their correlation with topographic variations and consequently with volcanic regions may also be evidence for internal convection. But correlations of gravity and topography could equally well be interpreted as the support of a topography by rigid material at depth. Finally, quasi-circular topographic features observed by Mariner 9 in the polar regions have been interpreted (B. C. Murray and M. C. Malin, unpublished) as evidence for polar wandering, which might also be expected if internal convection were active on Mars.

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Plutonic or Metamorphic Equilibration in Apollo 16 Lunar Pyroxenes

A FELDSPATHIC microbreccia from the Descartes region of the lunar highlands contains an unusual assemblage of pyroxene fragments. The numerous angular grains exhibit striking subsolidus exsolution textures that indicate a very advanced state of equilibration between the participating phases. Previous work on the subsolidus behaviour of lunar pyroxenes has been confined chiefly to submicroscopic exsolution. This required resolution by X-ray diffraction analysis which could not provide the specific major and minor element compositions of each phase.

The implications of finding textures of this type depend upon two alternative hypotheses. Some strongly zoned basaltic lava pyroxene crystals may have been fragmented and then re-equilibration of the fragments occurred at relatively high metamorphic temperatures during microbreccia formation, say in ash flow. Alternatively, a thick, fractionated plutonic complex has been disrupted from within the primitive lunar highlands crust, and the pyroxene exsolution developed within that pluton has been preserved within the microbreccia formation. We prefer the latter hypothesis.

Two polished thin sections (67075,43 and 67075,48) have been examined. The rock sample (219 g) was collected during the Apollo 16 mission, from the southeast rim of North Ray crater. It is a feldspathic microbreccia in which both clasts and matrix are very rich in fragmented, calcic

Fig. 1 Photomicrograph of thin section of Apollo 16 microbreccia (67075,48). The two high relief grains in the field centre are of coarsely exsolved pyroxenes (see Fig. 2 for enlargement of the larger grain). Most of the material shown is of brecciated calcic plagioclase feldspar, feldspathic clasts and dark, finely crushed areas.

plagioclase (An96 to An97). The exsolved pyroxene fragments are distributed evenly, both within and outside the shadowy and ill-defined clasts. The total pyroxene content is only about 4% by volume, but the textural characteristic (Fig. 1) is found in more than 50 detectable grains. Olivine occurs as rounded grains with dark, cloudy reaction rims, the composition being uniform at Fo44. Rare opaque minerals include ilmenite and chrome-spinel, both with low Mg/(Mg+Fe) of 0.06. The total non-feldspathic component is less than 8% by volume.

The commonest pyroxene size is 200–300 μm, each pyroxene being an angular crystal without evidence for marginal remelting or reaction with the enclosing matrix. The example given in Fig. 1 shows characteristic lamellae orientated on the (001) plane of the host crystal which shows cleavage traces parallel to the c-axis. The larger grain is shown enlarged and under cross-polars in Fig. 2. There, the host pyroxene has additional (100) exsolution, parallel to the cleavage traces. Another crystal (Fig. 3) shows, in addition to coarse exsolution on (001), fine-scale exsolution on (001) within the pyroxene phases. These two examples are typical of most grains. An additional variety, however, occurs as an orthopyroxene host with rare, irregular blebs of higher birefringence clinopyroxene. All examples are strongly reminiscent of subsolidus exsolution textures within pyroxenes from terrestrial layered basic intrusions, such as the Skaergaard and Bushveld.

The compositions, in terms of the principal element variables (electron probe anlysis), are plotted on Fig. 4. Each pair of analysed points, joined by a tie-line, represents the alternating coarse lamellae within a single grain. In most cases (Fig. 3) it is not possible to distinguish between host and lamella, but the compositional nature of the lamellae was characterized in each case, and a modal count made to determine the bulk composition of each grain before exsolution. This method needs refinement, so the semi-quantitative bulk compositions are not plotted on Fig. 4.

Two features of special interest emerge from Fig. 4. First, the alternating lamellae have been equilibrated at subsolidus temperatures to a remarkable extent. Both the Ca rich and Ca poor phases plot at nearly constant calcium

Fig. 3   Photomicrograph, under crossed polars, of a subcalcic augite (bulk composition) with coarsely exsolved calcium rich and calcium poor phases (the compositions of the two phases are the most Mg rich pair on Fig. 1; see also Table 1, analyses 1A and 1B). Note also the fine-scale exsolution parallel to the coarser (001) lamellae. Sample 67075,43.

contents, the compositional ranges paralleling the joins diopside-hedenbergite and enstatite-ferrosilite (Ca43 and Ca2, respectively, in Fig. 4). The lengths of each tie-line must, therefore, approximately define the gap between the two solvus limbs within this system at the lowest temperature of equilibration. For comparison, two exsolved pyroxenes from the Bushveld intrusion[1] are shown on Fig. 4. One pair represents an exsolved augite with clinohypersthene lamellae and the other an exsolved pigeonite inverted to hypersthene with augite lamellae. Both phases occur in the same gabbroic rock and are believed to represent extreme equilibration during very slow cooling of this vast intrusive body. The temperatures are difficult to estimate in the

Fig. 2   Photomicrograph, under crossed polars, of calcium poor pyroxene with coarse lamellae of calcium rich pyroxene (the compositions of the two phases are the most Fe rich pair on Fig. 4). In this case a pigeonite crystal exsolved augite on the (001) plane became clinohypersthene by re-equilibration with the lamellae on further subsolidus cooling, and exsolved more calcic pyroxene as the fine lamellae on (100), parallel to the visible (110) cleavage traces. Sample 67075,48.

Table 1   Electron Probe Analyses of Pyroxene Exsolution Lamellae from Sample 67075

	1A	1B	2A	2B	3A	3B
SiO_2	53.34	52.52	51.33	51.55	50.44	51.49
TiO_2	0.11	0.17	0.23	0.39	0.26	0.57
Al_2O_3	0.52	0.73	0.44	0.80	0.20	0.86
FeO	21.34	9.68	27.34	12.44	32.12	14.73
MnO	0.38	0.14	0.55	0.30	0.60	0.39
MgO	22.96	15.27	18.39	13.00	14.70	11.27
CaO	1.14	22.14	1.15	20.71	0.98	20.40
Cr_2O_3	0.21	0.26	0.23	0.24	0.22	0.33
Total	100.00	100.91	99.66	99.43	99.52	100.04

Unit formulae:

	1A	1B	2A	2B	3A	3B
Si	1.980	1.950	1.974	1.962	1.988	1.967
Ti	0.003	0.005	0.007	0.011	0.008	0.016
Al	0.023	0.032	0.020	0.036	0.009	0.039
Fe	0.663	0.301	0.879	0.396	1.059	0.471
Mn	0.012	0.004	0.018	0.010	0.020	0.013
Mg	1.271	0.845	1.054	0.738	0.864	0.642
Ca	0.045	0.881	0.047	0.845	0.041	0.835
Cr	0.006	0.008	0.007	0.007	0.007	0.010
O	6.000	6.000	6.000	6.000	6.000	6.000

Atomic ratios:

	1A	1B	2A	2B	3A	3B
Fe	33.49	14.83	44.39	20.02	53.91	24.17
Mg	64.22	41.70	53.22	37.29	43.98	32.96
Ca	2.29	43.46	2.39	42.70	2.11	42.88

Paired sets are selected as relatively Mg rich (1A–1B), intermediate (2A–2B) and Fe rich (3A–3B), as shown in Fig. 1.
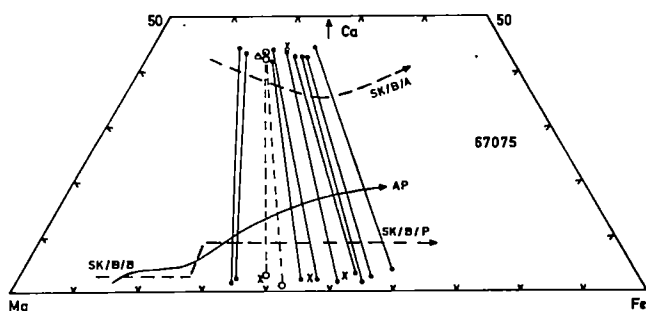
Fig. 4 Plot of the Ca-Mg-Fe contents of analysed, subsolidus-equilibrated pyroxenes in the quadrilateral $CaMgSi_2O_6$–$CaFeSi_2O_6$–$Mg_2Si_2O_6$–$Fe_2Si_2O_6$. The solidus assemblage trends for comparable pyroxenes are shown for Skaergaard and Bushveld augites (SK/B/A), bronzites (SK/B/B) and pigeonites (SK/B/P), and for lunar Apollo pigeonites (AP). ●—●, Lamellar pairs; ×, one-phase fragments; △, inclusion in plagioclase; ○, terrestrial (Bushveld) lamellar pairs.

absence of experimental data within the pyroxene quadrilateral, but "annealing" at about 900° C would be a likely estimate.

A second feature is the wide range in Mg:Fe ratios between pairs (Fig. 4). The orientation of the tie-lines provides a crude estimate of the distribution coefficient (K_D) for Mg and Fe^{2+} between coexisting Ca rich and Ca poor pyroxenes[3]. It has usually been assumed that the value of K_D is a guide to the temperature of equilibration between paired compositions, lower temperatures leading to successively decreasing values. This would be represented graphically by a rotation of the tie-lines (Fig. 4) in an anticlockwise direction with decreasing temperatures of equilibration*. Instead, the subsolidus assemblages plot on similar tie-lines to the solidus pairs[1], suggesting that subsolidus re-equilibration is achieved by calcium redistribution between the exsolved phases and is not accompanied by observable Mg and Fe^{2+} redistribution. So the K_D values for the Apollo 16 pyroxene assemblage do not provide the desired guide to temperatures of equilibration. Instead, they give values of about 0.6–0.7 which are identical to those of the Bushveld exsolved assemblage, but also to the Bushveld higher-temperature solidus assemblage[2]. The most dependable evidence for re-equilibration (Fig. 4) includes the trends for solidus assemblages from terrestrial augites and pigeonites; the extent of subsolidus re-equilibration can be gauged from the displacement of the plotted points, giving "stable" trends with constant Ca values for all the sets of pairs.

It is important to remember that the plotted pairs on Fig. 4 are for subsolidus lamellae. The semi-quantitative estimates of bulk compositions chiefly indicate, first, augite bulk compositions, exsolved to a calcic augite host with (001) lamellae of clinohypersthene; and second, pigeonite bulk compositions, exsolved to a clinohypersthene host with (101) lamellae of augite. The principles for very similar terrestrial occurrences are discussed elsewhere[1,3].

The chief point is that an original assemblage of Ca rich and Ca poor pyroxenes, varying widely in Mg:Fe^{2+} ratios, has been re-equilibrated at subsolidus temperatures in either a plutonic or a metamorphic environment. The Ca poor subsolidus assemblage is displaced far from the general trend of lunar Ca poor pyroxenes (AP, Fig. 4) and the same is true of the Ca rich assemblage. But lunar basalt pyroxenes show complex solidus compositional relations within the pyroxene quadrilateral, and it is just possible that the assemblage we are considering is of metamorphosed crystals with strongly contrasted bulk compositions, derived from fragmented, zoned basaltic lava pyroxenes. Lack of support for this lava-derivation hypothesis comes from the minor element analyses. Three examples of pairs, given in

* Lengths of tie-lines and Mg:Fe ratios, however, complicate this over-simplified concept.

Table 1, show the usual type of equilibrated distribution[1] of Al, Ti, Cr and Mn between the Ca rich and Ca poor lamellae. They also show, however, extremely low values for Al and Ti in both types of lamellae (and hence in bulk compositions) compared with any of the thousands of lunar pyroxene analyses now available (Fig. 5).

A metamorphic process would be more conventional, in terms of present ideas on the microbreccias having been annealed in hot ash flows at 600° C or higher. The difficulties in accepting such a hypothesis are, however, appreciable. The wide range in pyroxene Mg:Fe ratios within a single slice of breccia would require that the source crystals were strongly zoned on a coarse scale, and fragmented roughly parallel to zonal interfaces. The processes of fragmentation (by meteoritic impact) and annealing would be separate events, for otherwise the annealing would have homogenized the zoned crystals before producing the subsolidus exsolution. Finally, the pyroxenes so far analysed from lunar basalts, microbreccias or soils do not show the low Al contents of this assemblage, and a unique source is therefore to be sought.

The simplest explanation for the observation would be to draw an analogy with strongly fractioned, terrestrial layered intrusions. There the Ca rich and Ca poor pyroxenes show a regular decrease in Mg:Fe^{2+} ratios with lowering solidus temperatures. They also show subsolidus exsolution identical in textures (although coarser) and compositional effects to those shown in the lunar crystals. The disruption of a fractionated plutonic complex, situated within the lunar crust, is therefore a reasonable possibility. Plagioclase was probably a co-precipitating phase because small pyroxenes within plagioclase crystals show the low Al, as well as the subsolidus equilibration effect, shown by the other grains (Figs. 4, 5). The ferriferous olivines could have coexisted with the more ferriferous pyroxenes shown in Fig. 4, the more magnesium pyroxenes having been precipitated from tholeiitic type liquids with which more magnesium olivines were unstable.

The microbreccia is from an ancient highlands formation on the Moon, so the pyroxene fragments must have been derived from an even older Pre-Imbrian complex. The pyroxenes are unlikely to have been derived directly from lunar mantle pyroxenite material, in view of their wide range in Mg:Fe ratios. Compelling evidence for localized ancient plutonic complexes on the Moon lies in the existence of granitic rocks in the ancient breccias, and of troctolitic fragments with ultra-basic compositions. We believe that
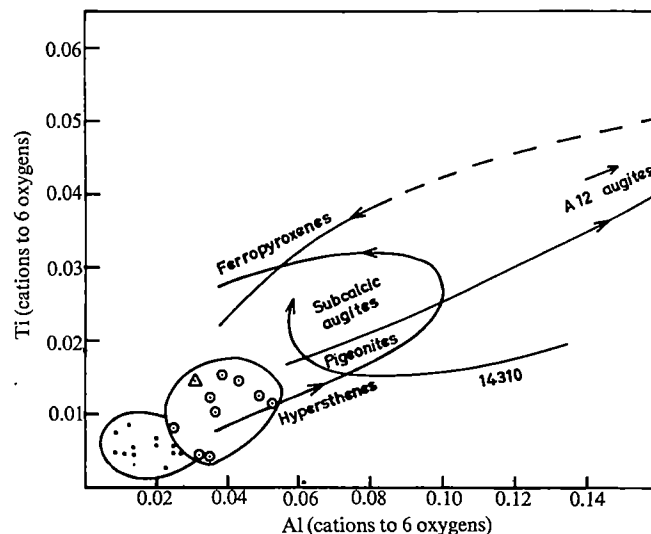
Fig. 5 Plot showing the low aluminium and titanium contents of the analysed pyroxenes, compared with generalized trends for other lunar pyroxenes, including those from a feldspathic lunar basalt (14310). ●, Ca poor lamellae; ○, Ca rich lamellae; △, Ca rich crystal in plagioclase.

much remains to be learned about the early pre-mare magmatic history of the Moon from a study of exotic mafic fragments from both recent and earlier mission collections.

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The Thickness of Deep Seismic Zones

Seismic ray tracing[1-4] has shown that the slabs of lithosphere which descend into the mantle in subduction zones are approximately 80 km thick. Within these slabs there are thin zones in which earthquakes occur[5]. Here I estimate the thickness of the seismic zone in Tonga as ~11 km, from the source dimensions of the large intermediate earthquakes.

From hypocentre locations, the thickness of the seismic zone has been estimated to be at most 25 km in the Tonga area[6,7] and approximately 10 km in Southern Alaska[8] and the Central Aleutians[9]. Because the hypocentre determinations are still affected by considerable errors it has been suggested[6,7] that the deep earthquake zone may be as thin as 5 km.

Hypocentre locations give an upper limit for the thickness of the seismic zone, but source dimension estimates for individual earthquakes provide a lower limit. The whole of the failure area of an earthquake must be contained within the seismically active part of the slab. The minimum estimate is possible because the two conjugate fault planes typically cut across the brittle zone at 45° angles[19] (Fig. 1). Thus the width of either of the two planes perpendicular to the slab is equal to the thickness of the seismic zone divided by $\cos(45°)$. In the direction parallel to the strike of the slab the fault plane could be elongated, but spectral observations show that except for the largest earthquakes the source areas are approximately circular[15]. From first motion studies it is evident that all earthquakes can be modelled as double couple sources. Fukao[10] and Abe[11] have made strong cases for two deep earthquakes to have been dislocations on a plane. I therefore take the focal mechanism of non-shallow earthquakes to be a failure on a plane.

For four earthquakes for which the source area was known from surface faulting and aftershock locations, the source dimensions have been estimated from seismic spectra[12,13]. The dimensions derived from spectra exceeded the field observations by 8 to 25%. If this comparison is also valid for deep and intermediate earthquakes the source dimensions of deep earthquakes can be derived with accuracies of approximately 30%. Because the source dimensions are about 10 to 20 km the proposed method to determine the thickness of the brittle zone is competitive with the hypocentre locations. In some oceanic areas where near stations cannot be deployed the accuracy of hypocentre locations may never be better than 10 km. In these areas the proposed method may remain the most accurate way of estimating the thickness of the deep seismic zone.
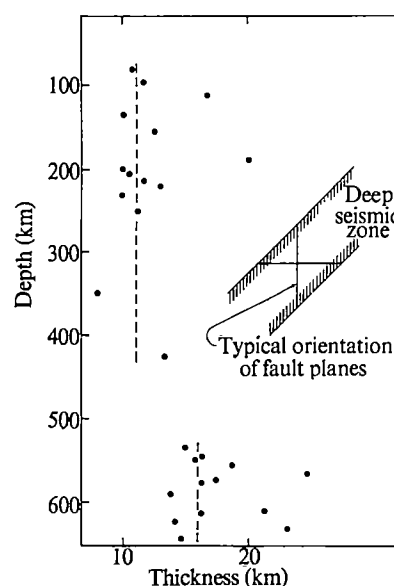
Fig. 1 Thickness of deep seismic zone in Tonga. ●, Estimates based on source dimensions of individual earthquakes[15]. Inset shows geometry of typical fault planes.

In the Tonga-Kermadec and other regions it was found that the source dimensions of earthquakes with $m_b \geq 5.6$ were fairly constant for focal depths between 70 and 700 km (refs. 14, 15). This surprising result, together with the constant width of the hypocentre scatter as a function of depth, suggests that the limitation on the source dimensions is imposed by the thickness of the deep seismic zone and that the large earthquakes extend across the whole width of the deep seismic zone. In that case the source dimensions provide not a minimum but a true estimate of the thickness of the brittle zone. The lack of extensive aftershocks at depth also supports this idea and may be partly explained by a model where the failure extends across the seismic zone, ending on either side at what may be considered a free surface because the material beyond it will deform by creep in response to stress. Aftershocks would still be expected in directions parallel to the strike of the deep seismic zone.

I therefore suggest that the source dimensions of magnitude 6 earthquakes indicate the thickness of the deep brittle zones. Fukao[10] has proposed that the largest earthquakes break across the slab. I believe that the few gigantic deep earthquakes which have approximately double the source dimensions of all the other large events[15] may be explained by especially thick portions of the brittle zone, or by fault planes more nearly parallel to the dip of the zone, as is the case for the event studied by Abe[11].

Fig. 1 shows the estimated thickness of the brittle zone in the Tonga as a function of depth. The thickness of the deep seismic zone is 11 km at intermediate depths. This value is close to the thickness of the seismic zone under Southern Alaska[8]. Around 600 km depth the seismic zone in Tonga is distorted[7] and the source dimensions indicate a thickness of 16 km.

The lithosphere under the oceans is estimated to be 70 km thick[16]. The brittle part is again much thinner and confined to the very top layers. At the ridge crest where the crust is produced, the brittle part is thinner than 5 km, which is approximately the cutoff depth for hypocentres in Iceland[20]. Source depths on the San Andreas Fault and slip-rate comparisons on other transform faults[17] indicate that the brittle crust is between 1 and 10 km thick at transform faults some distance away from the spreading centre. Below the Tonga trench the thickness increases to 11 km in the straight part of the slab and 16 km in the bent and possibly buckled part at great depth. This suggests that the thickening of the

brittle crust occurs fairly rapidly near the ridges, which is in agreement with the estimated geothermal gradients there[18].

It seems that farther away from the ridge crest the brittle crust remains constant in thickness over great distances.

I conclude that the size of deep and shallow earthquakes is limited by the thickness of the brittle crust. Very large earthquakes are only possible on planes dipping nearly like the brittle crust, that is, in the mega thrusts of subduction zones.

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Deposition of Sulphur Dioxide on Grass

SULPHUR dioxide may be removed from the atmosphere in rain, by oxidation resulting in particulate material, or by direct interaction of the gas molecules with the lower boundary of the atmosphere. The last mechanism is known as dry deposition and is independent of the nature and condition of the surface. This communication reports the first results of a programme of measurements of the dry deposition of sulphur dioxide studied by two separate methods.

In the first method the variation of concentration χ of sulphur dioxide with height z is measured. Because of deposition at the surface and eddy diffusion in the atmosphere the concentration decreases toward the surface and the flux is given by

$$F = K(z)d\chi/dz \qquad (1)$$

where $K(z)$ is the eddy diffusivity for sulphur dioxide. Thus F can be obtained from simultaneous measurements of $K(z)$ and $d\chi/dz$. We assume that the eddy diffusivity for sulphur dioxide approximates that for momentum, K_m. K_m can be estimated from the profiles of wind speed and temperature provided that measurements are made close to a large horizontal uniform surface where the constant-stress assumption applies. The site used was a grass field on chalky soil offering a fetch of 150 or 200 m in the upwind direction.

Sulphur dioxide concentrations were measured at heights of 0.2, 0.5 and 1.0 and 2.0 m. Air was drawn at 30 l. min^{-1} for

periods of 60 to 120 min through sampling trains comprising, first, heated polystyrene (microsorban) filters which remove particles but not sulphur dioxide and, second, glass bubblers containing hydrogen peroxide solution.

The sulphur dioxide trapped in the bubblers was determined as sulphate by the method due to Persson[1]. The wind speed was measured at five heights from 0.25 to 2 m using cup-anemometers and the air temperature was measured up to 4 m with platinum resistance thermometers.

The weather was cloudy and buoyancy effects were small in most cases, so the wind speed $u(z)$ was fitted graphically to

$$u(z) = u_* \ln((z-d)/z_0)/k$$

where d is the zero displacement, z_0 the roughness length, u_* the friction velocity and k Von Karman's constant. The eddy diffusivity $K_m(z)$ at 1 m could then be calculated because

$$K_m(z) = k.u_*(z-d)$$

In two cases when the heat flux was not negligible a correction (of the order of 10%) was derived by calculating the Richarson number and using the results of Businger[2].

The sulphur dioxide concentration was also plotted as a function of height to obtain the gradient of concentration at 1 m so that the flux F could be calculated using equation (1) and the deposition velocity $v_g = F/\chi(1)$ obtained.

In the second method a small amount ($\sim 10^{-3}$ mol) of sulphur dioxide containing 30 mCi of ^{35}S was released at a height of 1 m at a position 100 m upwind of the sampling section, a marked area near the centre of the field. The concentration in air was measured above the crop using peroxide bubblers from which an aliquot was taken for liquid scintillation counting. The flux of $^{35}SO_2$ to the crop was measured by sampling several measured areas of the crop. The ^{35}S content was determined by extraction of total sulphate and liquid scintillation counting, and the deposition velocity was calculated from $v_g = F/\chi(1)$.

Simultaneous measurements of the wind speed profile enabled the roughness length z_0 and friction velocity u_* to be determined.

The results, presented in Table 1, show the deposition velocity for each measurement. Also shown is the resistance for deposition, $r = 1/v_g$. The resistance may be considered as the sum of resistances acting in series:

$$r(z) = r_a(z) + r_s$$

where r_a is the aerodynamic resistance and r_s the surface resistance. The latter reflects any departure of the surface from perfect sink behaviour and must depend on the nature and condition of the surface. We can calculate r_a from the wind profile allowing for the difference between mass and momentum transfer using the sublayer Stanton number of Owen and Thomson[3]. An estimate of this parameter for sulphur dioxide was made from the work of Chamberlain[4] and Thom[5]. The calculated value of r_a was subtracted from r to determine r_s (Table 1).

The surface resistance, r_s, is generally a significant part of r showing that the surface cannot be considered a perfect sink. The values of r_s obtained by the two methods cover a similar range, varying by more than an order of magnitude, but no obvious relationship between r_s and the prevailing conditions emerged. In view of the suggestion of Cowling and Jones[6] that sulphur dioxide fulfils an important role compensating for sulphur deficiency in the soil, and because of its significance as an air pollutant, it is of interest to consider the long term deposition rates implied by the results. Using the average of the fifteen determinations, $v_g = 0.0085$ m s^{-1}, a mean concentration of 40 µg m^{-3} (ref. 7) in country districts would yield a deposition rate of 110 kg of sulphur dioxide per hectare year or, if a further extrapolation is justified, 1.9 Mton yr^{-1} over the country as a whole. This is nearly 40% of the annual produc-

Table 1 Measurements of the Deposition Velocity of Sulphur Dioxide on Grass

Date	Concentration $\chi(1)$ μg m^{-3}	u_* m s^{-1}	$u(1)$ m s^{-1}	z_0 m	v_g m s^{-1} Mean	v_g m s^{-1} Error	r s m^{-1}	r_s s m^{-1}
Radioactive tracer method								
June 8, 1972		0.63	4.8	0.040	0.022	±0.0005	45	20
July 17, 1972		0.40	4.5	0.010	0.0036	±0.0003	280	230
August 29, 1972		0.40	4.1	0.014	0.0094	±0.0018	106	66
September 14, 1972		0.37	3.8	0.024	0.017	±0.002	59	11
October 18, 1972		0.38	3.8	0.026	0.0076	±0.0007	130	76
November 2, 1972		0.27	2.7	0.014	0.012	±0.0014	83	20
Gradient method								
November 22, 1972	12	0.29	3.3	0.0105	0.0079		130	65
November 22, 1972	21	0.21	2.3	0.0115	0.0069		150	64
December 13, 1972	36	0.29	3.3	0.0105	0.0086		110	53
December 21, 1972	34	0.053	0.60	0.012	0.0016		610	330
December 21, 1972	71	0.084	0.85	0.012	0.0025		400	220
January 11, 1973	20	0.25	2.7	0.012	0.0093		110	37
January 11, 1973	14	0.30	3.4	0.009	0.013		77	15
January 12, 1973	20	0.24	2.6	0.012	0.012		86	14
January 12, 1973	26	0.24	3.0	0.006	0.0073		140	58

tion of 5 Mton and more than twice the 0.7 Mton yr^{-1} deposited by rain.

It is evidently desirable to extend the measurements reported here to a wide variety of surfaces, so that the influence of dry deposition on the long distance travel of sulphur dioxide may be determined. It is already clear, however, that dry deposition is an important mechanism for the removal of the gas from the atmosphere.

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Generation of Chemical Waves

A RECENT communication on the generation of spatial waves by the Zhabotinskii reaction[1], although reporting interesting experimental results, unfortunately propagates a serious error originally perpetrated by Busse[2]. This implies that periodic variations in space are possible for a simple linear autocatalytic reaction when diffusion of the autocatalytic species is taken into account. The steady state form of the equation in question is

$$D \frac{d^2c}{dz^2} + Kac = 0 \qquad (1)$$

where c is the concentration of autocatalytic species C, and a is the concentration (assumed constant) of another reactant A. The general solution of this equation is

$$c = C_0 \sin(2\pi z/\lambda + \varphi) \qquad (2)$$

where C_0 and φ are arbitrary constants and

$$\lambda = 2\pi(D/Ka)^{1/2}$$

In both refs. 1 and 2 boundary conditions are ignored; but

it is obvious that a sink for C (non-zero gradient) must be postulated at the walls of the container if a steady solution is to be possible, in order to compensate for the autocatalytic production of C within the volume. Otherwise there would be an explosion. In fact equation (2) has long been known as representing the free radical concentration in a chain branching system with heterogeneous wall termination[3]. Bursian and Sorokin[3] did not, however, interpret the sinusoidal form of the solution as representing waves of any kind because they realized that the only physically acceptable solution is one which is positive throughout the container, if it is to represent a concentration. Thus equation (2) is a physically acceptable solution only when the container dimension is less than or equal to half a wavelength; otherwise negative concentrations intrude. The sinusoidal solution then simply represents a distributed concentration for the species C and has no connexion with chemical waves at all. The same criticism applies to Rastogi and Yadava[1] except that they have transformed (incorrectly incidentally) into moving coordinates.

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Crystallographic Evidence for Ade-AdeH Hydrogen-bonded Pairs in a Cobalt-Adenine Complex

INTEREST in the role of metal ions in the biochemical reactions of nucleotides and nucleic acids[1] has led us to study the isolation of solid metal complexes with nucleotides and their bases, and to perform X-ray structural studies on suitably crystalline materials. In this way unequivocal information can be obtained concerning the preferred coordination sites of a given metal ion and also concerning the important question of hydrogen-bonding interactions in these systems. We report here the isolation of a crystalline complex of cobalt (II) sulphate with adenine (Ade) and details of its crystal structure.

Pale pink needles of composition [Co(H₂O)₄(Ade)₂](AdeH)₂-
(SO₄)₂.6H₂O (where AdeH represents the protonated aden-
inium cation $C_5H_6N_5^+$) were obtained from aqueous solutions
of adenine and cobalt (II) sulphate in 2 : 1 mol ratio. (Analy-
tical results: Found, C, 24.4; H, 3.8; N, 28.7; S, 6.6;
calculated, C, 24.65; H, 4.35; N, 28.8; S, 6.6%.) The
crystals are monoclinic, with unit cell dimensions $a = 13.971$,
$b = 7.190$, $c = 19.900$ Å, $\beta = 101.82°$, $U = 1956.6$ Å³, space group
$P2_1/n$ and $Z = 2$. The structure has been determined on the
basis of 2,275 independent reflexions measured on a Siemens
four-circle diffractometer using Cu-K$_\alpha$ radiation. Least-
squares refinement has now reached $R = 0.065$.

The structure contains the crystallographically centro-
symmetric $[Co(H_2O)_4(Ade)_2]^{2+}$ ion, AdeH and sulphate ions,
and molecules of water of solvation, all connected by an
intricate network of hydrogen bonds. In the complex cation
(Fig. 1) the cobalt atom has an octahedral coordination and
the coordinated adenine is monodentate, bonding via N(9), as
in [Cu(AdeH)₂Br₂]Br₂ (refs. 2, 3) while in Zn(AdeH)Cl₃ (ref. 4)
it bonds via N(7). In the other three metal-adenine complexes
whose structures have been determined hitherto, the inner
complex [Cu(C₅H₄N₅)₂H₂O]₂.6H₂O (ref. 5), [Cu(Ade)₂Cl]₂-
Cl₂.6H₂O (refs. 6, 7), and Cu₃Cl₈(AdeH)₂.4H₂O (refs. 8, 9),
adenine acts as a bridging ligand bonding via N(3) and N(9).
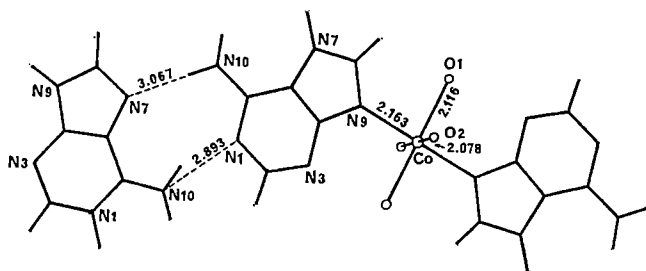
Fig. 1 A fragment of the structure showing the centrosymmetric
$[Co(H_2O)_4(Ade)_2]^{2+}$ ion and a hydrogen-bonded AdeH group.
Standard deviations are: Co-O, 0.005; Co-N, 0.005; and
N···N, 0.009 Å.

We have been able to locate unequivocally the positions of
the hydrogen atoms for both the Ade and AdeH moieties, and
have indicated them in Fig. 1. The hydrogen bond network
found in this structure contains the following types of bond:
O-H...O, N-H...O, O-H...N, N-H...N, and possibly
C-H ... O. The full structural details will be published
elsewhere.

Another feature of this structure which is of some biological
interest is the presence of hydrogen-bonded pairs Ade-AdeH
oriented as shown in Fig. 1. Of the two N-H ... N hydrogen
bonds joining the pair N(10)-H ... N(1) is the shorter one.
A similar connexion of Ade units is found in 9-methyladenine[10]
and in deoxyadenosine monohydrate[11]. These, however, form
an infinite zigzag chain whereas in this structure the interaction
is limited to a discrete pair because of protonation at the
crucial N(1) site in AdeH.

Although caution should be exercised in making an extra-
polation to complex biological systems, it is conceivable that
if under certain conditions an individual adenine base in a
nucleic acid becomes protonated, then this may help to stabilize
an abnormal adenine-adenine pairing. The rare, even tran-
sient, formation of such a linkage followed by normal replica-
tion provides one simple mechanism for a mutation, where in
this case Thy is substituted for Ade in the DNA sequence.
This abnormal pairing may also occur in the transcription
stages involving RNA, the end product in each case being a
single erroneous amino-acid in the peptide sequence or an
aberration in the chain termination process.

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On Boiling an Egg

Dwek and Navon[1] give the temperature of boiling water on
the top of Pike's peak as 91° C; at an altitude of 14,110 foot
the atmospheric pressure should correspond to a boiling
point of 86° C. I can, however, confirm their observations
from experimental results obtained at 7,300 foot (93° C boiling
point); these indicate that an egg may be hard-boiled in 12
minutes. My results support these authors' contention that
considerably less than 12 h is required, either at 91° or 86° C,
to hard-boil an egg.

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BIOLOGICAL SCIENCES

Isolation of the Islets of Langerhans for Transplantation

PANCREATIC transplantation with the aim of treating diabetes
mellitus has so far met with little success. Of 23 patients thus
treated and reported to the Transplant Registry in 1971[1], 15
died within 3 months and the longest survived one year. One
of the major problems has been to overcome pancreatic
exocrine digestion, and pancreatic duct ligation ("Banting
pancreas") before transplantation has been performed. It was
shown by Dragstedt[2], however, that dogs treated in this way
often became diabetic or showed a diabetic glucose tolerance
test after several months, probably due to fibrosis and conse-
quent ischaemia of the Islets. Transplantation of the whole

gland with its vascular supply is a major undertaking and the problems of thrombosis, leakage and digestion, coupled with immunological rejection, have prevented success so far.

Attempts have been made to isolate the Islets of Langerhans from the pancreas in order to study glucose metabolism. A micro-dissection technique was described by Hellerstrom[3] but this was tedious and produced only small numbers of Islet clumps. Subsequently Moskalewski[4] described a method of collagenase digestion which was successful in the rabbit and improved the yield, and Lacy and Kostianovski[5] modified the method for the rat. There were still difficulties in harvesting the liberated Islets, however, even with methods of separation such as zonal centrifugation and density gradients, and there were also problems with viability of the cells.

We have developed a technique by which large numbers of Islets of Langerhans are prepared consistently from the rat pancreas for purposes of transplantation. Viability was confirmed by transplantation.

Initially, albino outbred rats and subsequently young adult inbred hooded rats (strain PVG/C) were used. Following killing by cervical dislocation, the ventral surface of the animal was shaved, prepared with chlorhexidine in spirit and the abdomen opened with a midline incision. Using a dissecting microscope, magnification × 10, a fine polyethylene catheter ('Intracath'—B. R. Bard, London) was introduced into the common bile duct and secured with a 2–0 linen thread ligature. The lower end of the duct was occluded with an artery forceps just before its entry into the duodenum. The pancreas was distended by injection of 10 ml. Hanks' solution containing bovine albumen (fraction V), 2 mg ml.$^{-1}$. It was found that after some practice this procedure could be completed within 5 min of the death of the animal. The pancreas was removed, transferred to a glass Petri dish, cut into small pieces with scissors and any excess fat removed. It was then transferred to a tube to which a further 10 ml. of Hanks' solution was added. The pancreatic tissue sank to the bottom and any remaining fat floated on the surface and was readily aspirated and discarded. The prepared tissue was transferred to a small conical flask together with 2 ml. Hanks' solution containing glucose 0.6 mg ml.$^{-1}$ and collagenase type 1 (Sigma Chemicals, London). The stoppered flask was placed in a shaking water bath at 37° C for about 30 min. The exact time for separation was determined by frequent sampling and examination under the dissecting microscope.

The digested pancreas was transferred to a tube and diluted with further cold Hanks' solution containing glucose in the same concentration as before and gently centrifuged for 1 min. The supernatant was discarded and fresh medium added, and the resultant suspension filtered into a Petri dish with a blackened base for examination under the dissecting microscope at × 10 magnification.

Initially the view was obscured by fine fragments of acinar
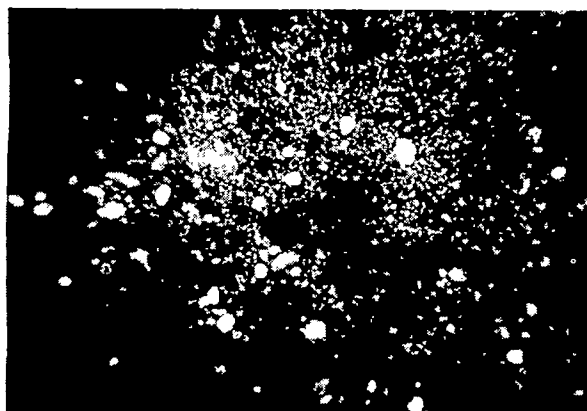
Fig. 1 Islet cell tissue seen after isolation from the pancreas using dark ground illumination. Dissecting microscope, × 5.
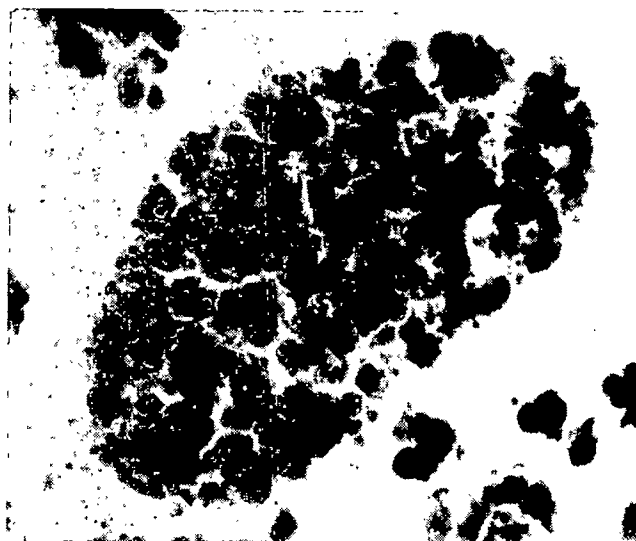
Fig. 2 Isolated pancreatic Islet. Normal architecture and appearance of cells. Haematoxylin and eosin, × 300.

tissue, which were removed by gently agitating the Petri dish and allowing them to become suspended in the Hanks' solution, then aspirated and discarded, the Islets remaining on the bottom of the vessel. They could then be seen clearly (Fig. 1) by the aid of dark ground illumination as yellowish white domes and were picked out with a finely drawn Pasteur pipette. Fig. 2 shows the histological appearance of an isolated pancreatic Islet. Its architecture and cells appear normal.

Yields of up to 350 Islets per rat pancreas have been achieved using this method. To obtain larger quantities, rat pancreases have been processed in batches of four.

Viability of the isolated cells was confirmed by transplantation beneath the renal capsule and into the testis of isogeneic rats. The longest period of follow-up was one month, when viable looking Islet cells containing beta cell granules staining with aldehyde-fuchsin were seen. A similar method has been successfully applied in the rabbit.

The relationship of the Islets of Langerhans to diabetes mellitus was established in 1889 by Von Mering and Minkowski[6], and in 1892 Hedon[7] demonstrated that subcutaneous implantation of a small piece of pancreas could delay the appearance of diabetes in an animal that had undergone pancreatectomy. The concept of Islet cell grafting appears to be neglected in the extensive literature on pancreatic transplantation, although one early report suggests that transplanted Islets may modify alloxan diabetes in the rat[8].

We have now established a successful method of isolation of Islets of Langerhans in an animal strain in which inbred immunologically isogeneic lines are available, making possible transplantation studies uncomplicated by rejection problems. These cells can be grafted and survive for appreciable periods of time as shown by the viability studies. Histological and functional studies of Islet cell transplantation will be reported elsewhere.

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Remarks on Virus-like Particles in Human Breast Cancer

MANY investigators have tried to correlate the genesis of human breast cancer with the presence of a virus. In spite of many electron microscopical studies[1,2], however, no convincing evidence of an association of human breast cancer with virus has been demonstrated. Last year, Moore and his colleagues[3] reported that they had found particles with the same morphological characteristics as those that cause breast cancer in mice (B particles), in the milk of 5% of the American women with no history of the disease in their families; in 60% of the Americans with a history of the disease in their families; and in 39% of Parsi women. Sarkar and Moore[4] distinguish the particles in human milk with a size and shape similar to the B particles into three classes: MS-1 identical to the B particles; MS-2 particles with the surface projections different from B, and MS-3 smooth particles. These results encouraged us to examine milk samples from Dutch women for the presence of virus-like particles.

Because our method of isolation of B particles from mice with mammary tumour virus (MTV)[5] is different from the method used by Moore et al.[6], the following preliminary experiments were performed in order to decide which isolation technique would be used. Small amounts of milk (0.05–1 ml.) from MTV infected BALB/c mice were added to 8-ml. samples of human milk. Each sample was divided into two equal parts. One part was treated according to the method of Moore and his coworkers and put on a two-step sucrose gradient (52% and 42%) followed by centrifugation on a continuous gradient of (5%–25%) Ficoll in phosphate buffered saline (PBS). Sometimes the centrifugation through Ficoll was omitted. The other half was treated according to our method and centrifuged on a four-step gradient of Ficoll and D_2O (Fig. 1a); as a buffer 0.01 M Tris (pH 7.0)+0.25 M sucrose was used. In solutions with

this sucrose concentration the infectivity of C particles is well preserved during sedimentation[7] and in our own experience the morphology of both B and C particles is better preserved than in PBS or other buffers. The use of Ficoll and D_2O as a gradient for isopycnic centrifugation has the advantage that the gradient is not hypertonic compared to the buffer system and thus an osmotic shock of the particles, during preparation, is avoided. The different fractions of each treatment were collected by puncturing the bottom of the tubes. Part of the material was pelleted and prepared for ultrathin sectioning; the rest was used for negative staining.

In three different experiments the added mouse B particles could easily be recognized in the material from the Ficoll/D_2O gradient both in negatively stained preparations (Fig. 1b) and in thin sections (Fig. 1c), even after a 1:80 dilution with human milk. This corresponds to the amount of virus in 25 μl. of mouse milk. Following the method of Moore et al.[6], we had more difficulties in finding mouse B particles in preparations after similar dilutions.

Because the preliminary test had shown that our own isolation method did not damage the structure of the B particles and may have the additional advantage of preventing an osmotic shock, this method was used in the following experiments. We examined forty-two milk samples (3–10 ml.) from women with no cancer history and one sample from a woman with a family history of breast cancer. After negative staining we always found three different types of structures in fractions 1 and 2 (Fig. 1a): (a) roughly spherical or elongated particles of different size that sometimes exhibited a fringe of fine projections ranging from 45 to 71 Å (Fig. 2a); (b) roughly spherical particles with an irregular electron dense inner structure and a thin periphery (Fig. 2b); (c) particles with a head and a tail that sometimes carried surface projections (like MS-2) (Fig. 2c). In fraction 3 (Fig. 1a), we found many smooth particles with a head and a tail that sometimes showed blebs (like MS-3) (Fig. 3).

The MS-3 particles found in large quantities in fraction 3 resemble negatively stained C particles. It is difficult to identify MS-3 as C particles for the following reasons: Milk is the product of an apocrine gland and may therefore contain cytoplasmic debris. Part of this debris (cell membranes) may assume, in negatively stained preparations, shapes with tail-like appendages similar to the C particles[8,9]. With the purification methods used not only all particles with the same density as B or C particles were isolated, but also, because of the limited centrifugation time, all particles with about the same size. For these reasons we correlated

Fig. 1 *a*, Schematic representation of partial purification for particles from human milk by isopycnic centrifugation on a Ficoll/D_2O gradient. *b* and *c*, Fractions of human milk to which mammary tumour virus-containing mouse milk has been added. *b*, A B particle after negative staining showing the typical spikes (arrow) (×168,000). *c*, Thin section of a B particle (arrow) with an excentric nucleoid surrounded by a membrane (×64,000).

Buffer: 0.01 M Tris pH 7.0 + 0.25 M sucrose

Gradient: Ficoll + D_2O

80 – 120 min 50 000 rpm

Spinco SW 50

d = 1.12

d = 1.14 → Fraction 3

d = 1.149 → Fraction 2

d = 1.165 → Fraction 1
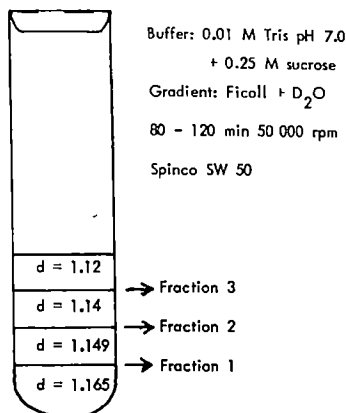
a
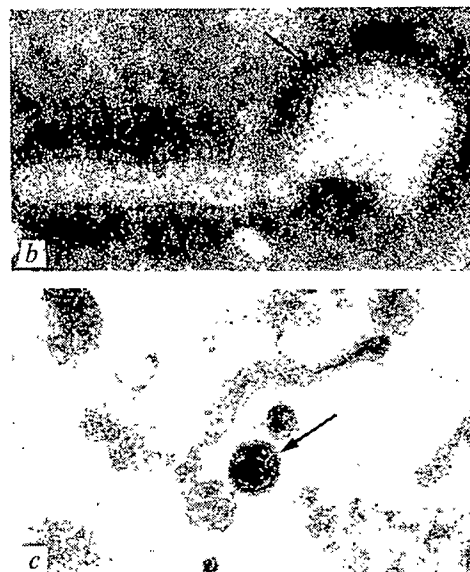
Fig. 2 Particles present in fractions 1 and 2 from human milk after negative staining. *a*, Particle with surface projections. *b*, Particle with an irregular electron dense structure that resembles the nucleoid of the oncornaviruses and with a smooth membrane (arrow). *c*, Particle with head, tail and remnants of broken projections (p) and the membrane (m). The head is broken at one side. (× 225,000.)
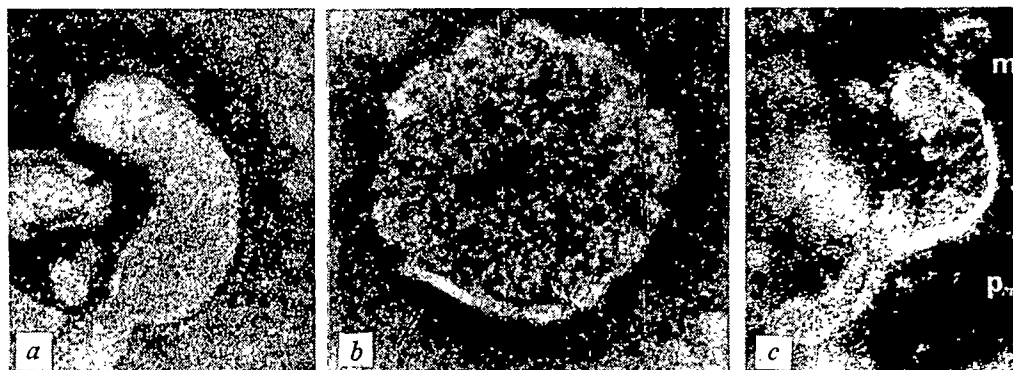
Fig. 3 Representative field of fraction 3 from human milk after negative staining. Two particles (arrows) resembling MS-3 type particles are shown; in one a bleb (b) is visible. (× 105,000.)
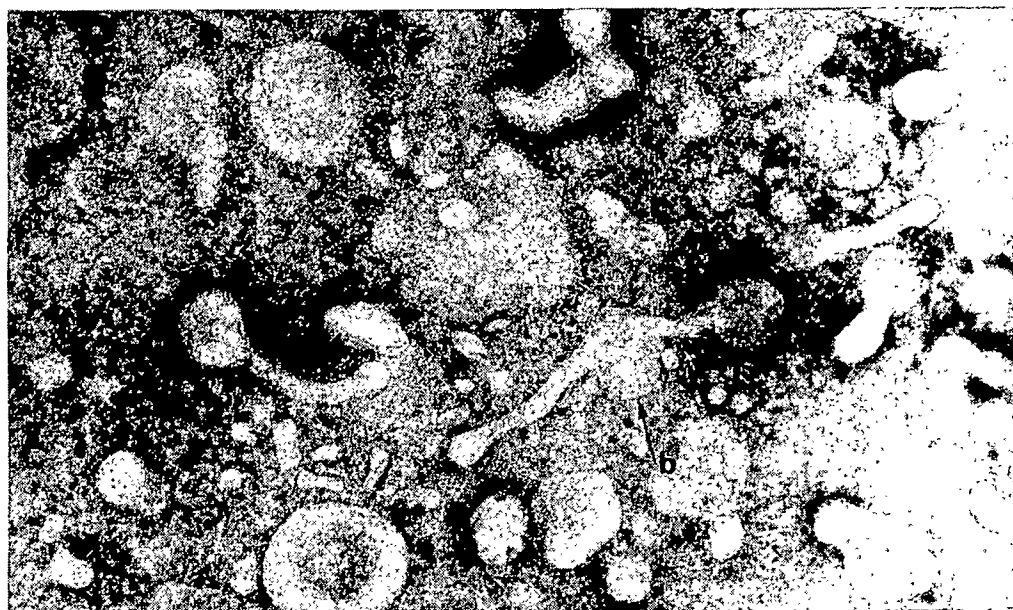
our results in negatively stained preparations with the study of the same material viewed in thin sections. If C particles were present it should be possible to identify them in thin sections by their nucleoid. However, no virus-like particles, neither of the B-type nor of the C-type, were found in thin sections.

Both in negatively stained material and in thin sections of the partially purified milk samples of forty-three women, the observed particles resemble those found by Jensen and Schidlowsky[10] in normal bovine and human milk. This indicates that these particles are present very frequently regardless of the source or type of milk, and makes it likely that they are cytoplasmic debris or secreted products from the mammary gland.

Sarkar and Moore[11] also reported five experiments in which five different human milk samples were mixed with mouse milk containing B particles. In three cases they found that the human milk altered the morphology of the B particles. We did the same experiment with six different human milk samples that were mixed, before removing the cream, with milk from MTV infected BALB/c mice. We were unable to find any damaging effect of human milk on the structure of B particles after incubation of the mixture at 37° C for 1 h. Only when the mixture was kept overnight at 4° C or 37° C did the amount of broken B particles increase, but this happened also in the control experiment when mouse milk from MTV infected BALB/c had been mixed with mouse milk from MTV-free BALB/c and the mixture was kept overnight at 4° C or 37° C. In several other experiments on MTV many B particles were damaged when mouse milk was kept overnight at 4° C.

Our investigation of the partly purified milk samples from

43 Dutch women has shown that: (1) no intact B particles nor intact C particles were found; (2) B particles from mouse milk were not morphologically influenced by substances from human milk in the cases reported here; (3) the different types of particles that were observed are probably cytoplasmic debris and secreted products from the mammary gland.

A human mammary tumour virus might not have the stability or the same morphology as the MTV of mice. Although both electron microscopical (compare Fig. 1*a*[3] and Fig. 3*a*[4]) and biochemical indications[12] exist for the presence of such a virus in human milk, one must be careful in correlating[4] the presence of rather unidentified particles like MS-2 and MS-3 in human milk with other characteristics like presence of RNA-dependent DNA polymerase or the breast cancer history of the family of the donor.

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Congenital Heart Disease and Maternal Smoking Habits

FEDRICK et al.[1] have produced data to show that the incidence of congenital heart disease in infants of mothers who are cigarette smokers is significantly higher than among infants of non-smoking mothers. In our child health development studies my colleagues and I have attempted to duplicate those findings which relate to their "control week" data. We used the same criteria, thus omitting all multiple births and all cases in which the defect was associated with anencephalus, spina bifida or Down's syndrome. We found no difference in the proportion of smokers and non-smokers between mothers of affected and unaffected children. Thus we found no difference between the children of smoking and non-smoking mothers with regard to the incidence of congenital heart disease (Table 1).

Our study was entirely prospective. The information on smoking was derived early in pregnancy, whereas in the study by Fedrick et al. the questionnaire was completed after delivery. Also, the children in our study were observed continuously and any suspected of congenital heart disease were given all appropriate tests, including electrocardiogram and

X-rays. Furthermore, at the end of the study all suspected children were examined and all records were reviewed by one paediatric cardiologist (Dr Julien I. E. Hoffman, University of California Medical Center, San Francisco). We were therefore confident that the final diagnoses were valid, and that the mothers' accounts of their smoking history were not biased by the outcome of their pregnancies.

The incidence of congenital heart disease among the infants of smokers was almost identical in our study and in that of Fedrick et al. (7.3% in their study, which is identical to the incidence among all races in our study, and very close to the 8.2% we obtained for whites). But we found a much greater incidence of congenital heart disease among the children of non-smokers (8.1 and 7.7 for all races and for whites, respectively, compared with 4.7).

After a thorough search of the literature, consisting of eighteen studies, four based on relatively large samples[7,8], I conclude that the findings of Fedrick et al. are at variance with most previous investigations, especially those based on relatively large samples (Table 2). Thus, contrary to the statement[1] that, "It is generally accepted that maternal smoking during pregnancy is associated with an increased risk of spontaneous abortion, low birth weight and stillbirth or neonatal death", the mortality rate is not greater for infants of smokers, and the perinatal mortality rate of low birth weight infants of smoking mothers is significantly lower than that of low birth weight infants of non-smoking mothers.

Table 1 Proportion of Smoking and Non-smoking Mothers of Children with and without Congenital Heart Disease (CHD)

Maternal smoking habits	Congenital heart disease				Live births without CHD			
	All races		Whites		All races		Whites	
	No.	%	No.	%	No.	%	No.	%
Smokers	38	33.0	31	39.7	5,158	35.3	3,735	38.1
Non-smokers	77	67.0	47	60.3	9,458	64.7	6,077	61.9
Total	115	100.0	78	100.0	14,616	100.0	9,812	100.0

Table 2 Perinatal Mortality* Among all Infants and Among Low-Birth-Weight Infants by Maternal Smoking Status in Four Studies of Large Sample

Study		Number of births	% low-birth-weight (≤2,500 g)		Perinatal mortality per 1,000			
					Total		≤2,500 g	
			Non-smoker	Smoker	Non-smoker	Smoker	Non-smoker	Smoker
Yerushalmy[2]	White	5,381	3.5	6.4	12.4	13.9	232.1	137.7
	Black	1,419	4.9	13.4	23.4	22.9	260.9	109.4
Underwood et al.[3]		48,505	5.7	8.9	19.7	20.8	269.0	187.0
Rantakallio[4]		11,931	3.5	6.1	23.2	23.4	343.6	287.6
Butler et al.[5]		16,994	5.4	9.3	32.4	44.8	284.5	268.5
Yerushalmy[6]	White	9,793	3.2	6.4	11.0	11.3	218.3	113.9
	Black	3,290	5.8	12.3	17.1	21.5	201.6	113.6

*Study of Yerushalmy refers to neonatal mortality only. A more complete review of all the evidence is given in the correspondence published in refs. 7 and 8.

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Reply to Professor Yerushalmy's letter on Congenital Heart Disease

WE were greatly interested in Professor Yerushalmy's data, for it is only by collecting information from many different sources that a finding can be substantiated epidemiologically.

Obviously any study in which, for example, the smoking history was obtained during pregnancy rather than after delivery is at an advantage. We believe, however, that the type of bias inherent in any retrospective survey is unlikely to have occurred to any marked extent in the present series because at the time of the inquiry there had been no publicity concerning the effects of smoking in pregnancy.

It is difficult to find any explanation (other than that due to chance) of the differences between the incidences of congenital heart disease (CHD) in the two populations of births. We would like to point out, though, that in our paper we had a second series of 204 cases of CHD among 7,000 perinatal deaths, and that the differences in incidence of CHD between infants of smokers and non-smokers were of the same order of magnitude as in our population series, even when variables such as maternal age, parity and social class had been allowed for.

As to the effect of smoking on perinatal mortality in general, we are somewhat surprised at Yerushalmy's interpretation of his Table 2 in which he states that the perinatal mortality rate in general is not larger for infants of mothers who smoke. In fact, of the selected studies he reports, and excluding Yerushalmy's 1964 sample which is a subsample of the 1971 sample, three studies show a very small increase in perinatal mortality and two studies show a large increase. Furthermore, he fails to mention the fact that all these studies give a similar estimate (150–200 g) for the average reduction in birthweight associated with smoking in pregnancy. Other studies[1] have shown that the reduction in gestation is only marginal, and we conclude that the effect of smoking is to produce a degree of foetal growth retardation. It is, however, irrelevant to compare the mortality rates of all infants under 2,500 g. Growth retardation although carrying a high risk of perinatal death is entirely different from low birth weight due to immaturity. The latter carries an even higher perinatal mortality death rate, and must obviously be considered separately.

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Marginal Vitamin B_{12} Intake during Gestation in the Rat has Long Term Effects on the Offspring

IT is now evident that malnutrition of the foetus or of the infant results in long term abnormalities in the physical, clinical and behavioural characteristics of the organism[1-4]. Experimental studies have generally dealt with the effects of severe malnutrition. There is reason to believe that less severe dietary imbalances, more likely to occur in population groups of the Western world, if imposed at an early stage, may have profound, adverse effects much later in life. Because the nutrient demands per unit of body weight are presumably higher in the foetus than in the newborn, a diet which is considered fully adequate for post-natal development does not necessarily provide, when consumed by the mother, an adequate nutritional environment for the developing foetus.

In previous studies[5] we observed that a high dietary level of B_{12} resulted in increased weight of the newborn compared with that of offspring from mothers receiving a basal diet in which the B_{12} level was somewhat in excess of the estimated needs for pregnant rats[6]. This latter dietary B_{12} level supports a normal or adequate birth weight in rats and permits a rate of post-natal growth which is considered to be within acceptable limits. However, based on the birth weight differences, our results suggested that the level of B_{12} in the basal diet represented a marginal deficiency of the vitamin and so we have explored its long term effects on the wellbeing of the offspring.

Pregnant rats received a dietary B_{12} intake (50 µg/kg diet) which somewhat exceeded the estimated requirement for the pregnant, lactating and growing rat[6], but which approximated a concentration often used in purified diets, or a level in considerable excess of this intake (50,000 µg/kg diet). Female rats (Sprague–Dawley, Charles River Laboratories) were housed in screen-bottom cages, given water *ad lib.* and fed from weanling on a basal diet. This diet contained (percentage by weight: 20.0 C-1 assay soybean protein; 28.9 glucose; 28.5 sucrose; cotton seed oil 15; choline 0.3; DL-methionine 0.3; salt mix 5.0; vitamin mix 2.0. Further details of diet have been described[7]. A supplement of crystalline B_{12} was added to the diet, at the time it was mixed, to achieve a concentration of 50 µg/kg of diet. At maturity, the female rats were placed in breeding units, three animals per cage. They continued to receive the basal, (control) diet and were bred to normal male rats of the same strain. Breeding was confirmed by a positive vaginal sperm smear. At this time, the female rats were transferred to individual cages and they were randomly allocated to receive the basal diet or the higher supplemental vitamin B_{12} level (50×10^3 µg/kg diet). Mean food intake during the 21-day gestation period was essentially the same in both groups: 454 g and 461 g for the basal and high B_{12} groups, respectively. Similarly, mean total weight gain during this period was 135 g and 128 g for the basal and high B_{12} groups, respectively. Two days after birth, litter size was reduced to eight and the mother was then fed the control diet until the young were weaned at 21 days. After weaning, the progeny continued to receive basal diet until they were used for various measurements. Although the higher levels of dietary B_{12} were given only during gestation it is recognized that the B_{12} supplied to the offspring born to mothers receiving the higher supplement of B_{12} most probably remained higher during lactation than those born to mothers given the control diet. Offspring were taken at various periods during the first year of life for assay of liver aminopyrine demethylase and glucose-6-phosphatase (EC3139) activity[8].

The latter was also visualized by histochemical means in both liver and kidney[9]. Enzyme assays were conducted on the livers of year-old rats which were fasted overnight and tissues collected for histological assessment[10]. To assess the possible clinical benefit gained from the increased B_{12} intake we utilized an experimental model previously described for study of the metabolic effects of a bacterial infection[11]. Rats were infected by oral administration with 5×10^9 organisms of *Salmonella typhimurium* at 3 months of age. Liver levels of B_{12} were determined[13] in representative female rats at time of conception and at littering and in the newborn for each diet group.

In agreement with our earlier findings, the higher dietary level of B_{12} during gestation did not affect litter size but significantly increased birth weight (Table 1). Body weight differences were still evident after 1 yr, demonstrating a long term influence of the higher dietary level of B_{12} provided during intrauterine life. Determinations of total body nitrogen and lipid revealed that the weight difference among the two offspring groups was reflected in a greater proportion of total

Table 1 Mean Values for Body Weight and Liver Enzyme Activity of Offspring born to Mothers receiving Two Levels of Dietary Vitamin B_{12} and for Liver Concentration of B_{12} in Dams and their Newborn

Parameter	Group Basal	Group High B_{12}
No. of litters	44	57
Litter size	9.7 ± 1.5‡	9.9 ± 1.2
Birth weight (g)	5.8 ± 0.2	6.2 ± 0.3 †
Body weight§ (g) at 21 days	41 ± 4	51 ± 3 †
3 months	351 ± 10	391 ± 11 *
1 yr	463 ± 9	510 ± 9 †
Liver enzyme activity‖:		
Glucose-6-phosphatase¶		
4 days	16 ± 2	24 ± 2 *
1 yr	60 ± 4	85 ± 6 *
Aminopyrine demethylase**		
4 days	28 ± 2	42 ± 3 †
1 yr	260 ± 9	340 ± 15 †
Liver B_{12} concentration:		
(ng B_{12}/g liver)		
Dam††	132 (90–160)‡‡	308 (234–417)
Newborn§§	27 (21–38)	68 (37–94)

*, † Significantly different at $P < 0.05$ and $P < 0.01$, respectively, from the basal group.
‡ Mean values $\pm$ s.e.m.
§ Weight of male offspring.
‖ Each mean based on twenty animals from ten litters.
¶ Activity expressed as μmol phosphate liberated/min/g, dry, fat-free liver.
** Activity expressed as μg aminoantipyrene formed/h/g, dry, fat-free liver.
†† Mean liver B_{12} concentration for ten females at time of conception was 173 (range 132–190). Values shown are at time of littering for ten females per diet group.
‡‡ Range of values given in parentheses.
§§ Values based on two animals from each of six litters per diet group.

body protein, as well as liver protein, and a lower proportion of total lipid for rats born to mothers who received the higher level of dietary B_{12}.

Liver B_{12} levels increased during gestation in the female rats receiving the higher B_{12} intake and decreased in those given the basal diet (Table 1). These changes were reflected by a higher concentration of liver B_{12} in the newborn from mothers receiving the high dietary B_{12} intake. Because total food intake during gestation was the same for each diet group, the differences in liver B_{12} concentrations and birth weights noted above, among the two diet groups, seem to be causally related to the differences in the dams' B_{12} intake and not to other dietary factors.

Table 1 also summarizes the *in vitro* activity of the two liver enzymes for the two time periods at which they were examined. Enzyme activity per unit of liver weight and per total liver was higher for rats born to mothers given the higher level of dietary B_{12}. These results may imply a greater capacity for handling foreign compounds entering the liver by way of the portal or peripheral circulation in rats born to mothers receiving the high dietary level of B_{12}.

The results of the *S. typhimurium* infection study are shown in Table 2. Eighteen hours after infection, positive cultures were found in blood samples in about equal numbers for both groups but bacteria were cleared more efficiently from circula-

Table 2 Effect of High Maternal Vitamin B_{12} during Gestation on the Response of Male Offspring to *Salmonella typhimurium* at 3 Months of Age

Parameter	Group Basal	Group High B_{12}
No. rats with positive blood culture:		
18 h after infection	16/20	18/20
48 h after infection	11/20	5/20
10-day cumulative mortality	21/40	9/40

tion within 48 h in rats born to the mothers receiving the higher supplemental level of vitamin B_{12}. Cumulative mortality for the first 10 days was lower in the offspring of the B_{12}-supplemented group indicating a greater resistance to the experimental infection. This experiment suggests a long term beneficial clinical effect on the offspring of the higher B_{12} intake during intrauterine development and that they responded more favourably to the stressful stimulus of a systemic infection.

Tissues taken from rats 3 days after infection and processed for histological and histochemical studies revealed a more marked increase in cellularity of the spleen of the high B_{12} group and a greater concentration of glucose-6-phosphatase in both liver and kidney. These differences are compatible with a more active and responsive metabolic apparatus in rats exposed to higher B_{12} *in utero*.

The basal level of dietary B_{12} utilized in these studies is sufficient to achieve a normal birth weight in the newborn, a storage of B_{12} in the liver at time of birth, and permits a rate of post-natal growth which is considered to be within a normal or acceptable range[6]. However, the findings show that an increased B_{12} concentration in the maternal diet during the gestation period results in a higher birth weight of the offspring, a higher concentration of liver B_{12} at birth and, more significantly, in an enhanced capacity of the organism to withstand stress in later life, based on the increased resistance to *Salmonella* infection. The findings suggest that an apparently mild deficiency of B_{12} may have subtle effects on the differentiation and functional development of the foetus. Furthermore, a marginally deficient nutrient supply at this critical phase in the life of the organism is clinically unremarkable in its effects until some time in later life and then only when the organism is challenged by a stressful stimulus.

These results underscore the potential adverse effects of a marginal maternal nutrient supply on the offspring but cannot be interpreted to mean that intake levels in excess of appropriate dietary standards are of any benefit. Our findings support the conclusions of others[13], that the effects of maternal nutrition during the prenatal period are carried over into the later life of the offspring, and they also parallel our previous observations[14] on the long term adverse effects of low-lipotrope diets during the gestation period.

We feel that the results of the present studies justify cautious consideration of their implications with regard to the nutrition of the human foetus and breast-fed neonate. Particularly important are those constituents which may be marginal in the mother's diet but without obvious manifestation in herself or of significance for the sibling until either are confronted by an additional stressful stimulus, such as infection and trauma or even during the metabolic changes which occur in response to pregnancy. Questions about many of the unexplained illnesses in children and the wide variation among individuals in their resistance to disease may conceivably be answered by more intensive study of the prénatal nutrient needs of mother and her foetus.

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Absorption, Accretion and Endogenous Faecal Excretion of Calcium by the Newborn Infant

MEASUREMENTS of calcium absorption require the administration of a suitable marker for natural calcium; the most commonly used markers in adults are ^{45}Ca and ^{47}Ca, two radioactive nuclides of calcium which cannot be used experimentally in infants because of the possible risk from radiation. Calcium salts enriched in the non-radioactive nuclides ^{46}Ca and ^{48}Ca are now available and may be used in newborn infants. Non-radioactive nuclides have the advantages that metabolic information can be obtained without exposure of the subject to ionizing radiation and that, if necessary, measurements can be made after prolonged storage of specimens because the marker is not subject to radioactive decay. The absorption, retention and elimination of calcium by the newborn infant are of practical importance[1] and here we provide measurements from which true absorption and endogenous faecal elimination can, for the first time, be inferred.

Four healthy but premature males (ages and weights given in Table 1) were fed from birth and during the tests on a carbohydrate modified cows' milk formula 1610F Ca (ref. 2). A solution containing 2.0 mg of Ca enriched in ^{46}Ca was added to a single normal feed and the intake of milk from this and subsequent feeds throughout the study was measured. Stools, urine and vomitus were collected for a total of 48 h and all specimens, including aliquots of milk, were dried and thermally ashed. The natural calcium content of specimens was measured by atomic absorption spectrophotometry and the ^{46}Ca content was determined from measurements of the radioactive ^{47}Ca produced during neutron irradiation of the specimens. Appropriate corrections were made for naturally occurring ^{46}Ca present in the specimens. Details of this method are given elsewhere[3].

We have assumed that the calcium marker and the natural calcium in the milk are equally available for absorption. Although for infants this has not been proved, for adults, the absorption of ionic and milk calcium is most probably equal when the two are ingested simultaneously[4].

Because exogenous excretion of the marker had virtually ceased within 24 h of administration, values could be obtained for true absorption, endogenous faecal excretion and accretion of calcium by applying the equations of Aubert *et al.*[5] to the measurements of natural and marker calcium. The results demonstrate the relatively small variation between four infants in the daily amounts of calcium absorbed (107–171 mg) and accreted (66–118 mg) from the milk used in these tests. The percentage absorption was constant (mean 33.8 ± 1.4), but the endogenous faecal excretion varied widely, from 0 to 20% of the intake. The difference in endogenous excretion between different infants may prove to be relevant to the aetiology of the calcium deficiency and calcium excess syndromes in the newborn[2].

Full term infants of the same age range but double the weight, fed on breast milk[6], ingested 45–48 mg Ca kg^{-1} day^{-1} on average, markedly less than the 217 mg kg^{-1} day^{-1} for the premature infants fed on the test formula. Retention in the breast-fed infants was 19–23 mg Ca kg^{-1} day^{-1} as compared with 50 mg kg^{-1} day^{-1} for accretion in the premature infants. There is clearly a need for further investigation of the factors, including dietary composition, which affect calcium metabolism in the human infant.

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Selective Synthesis of Liver Nuclear Acidic Proteins following Glucagon Administration *in vivo*

IT is known that the metabolism of the non-histone, acidic proteins associated with DNA in the chromatin of animal cells is influenced by steroid hormones. The effects are often highly specific; for example, the administration of hydrocortisone to adrenalectomized rats leads to a selective stimulation of synthesis of a liver chromosomal protein of molecular weight 41,000[1]. Hydrocortisone also alters the pattern of phosphorylation of chromosomal proteins in the liver, differential effects becoming evident within minutes after injection of the hormone[2,3]. Similar specific alterations in the synthesis or phosphorylation of nuclear proteins have been observed in uterine cells responding to oestrogens[4], in kidney cells following aldosterone administration (C. Liew, personal communication), in prostate cells stimulated by androgens[5], and in insect chromosomes stimulated by ecdysone[6]. In all these cases, the steroid hormone also affects the RNA synthetic capacity of the target cells, presumably as a result of altered template capacity of the modified chromatin.

Table 1 Intake, True Absorption, Accretion and Endogenous Faecal Excretion of Calcium by Four Premature Infants

Subject	Post natal age days	Weight kg	Mean daily intake mg	True absorption mg/day	True absorption % of intake	Endogenous faecal excretion mg/day	Accretion mg/day
L. N.	11	2.3	508	171	33.7	103	66
N. B.	10	1.9	435	161	37.0	46	109
M. M.	9	2.4	480	144	30.0	25	118
L. T.	41	1.5	311	107	34.4	0	105
Mean and s.e.	18 ($\pm$8)	2.0 ($\pm$0.2)	434 ($\pm$44)	146 ($\pm$14)	33.8 ($\pm$1.4)	44 ($\pm$22)	100 ($\pm$12)
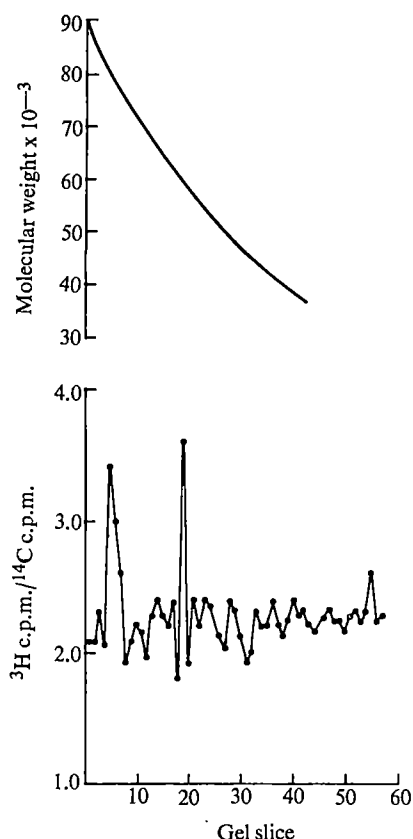
Fig. 1 Electrophoretic separation and radioanalysis of liver nuclear acidic proteins from glucagon-treated and control rats. Matched pairs of rats were injected with glucagon or saline solutions. Hormone-treated animals received 1 mCi of DL-4,5-^{3}H-leucine and control animals with 200 µCi of U-L-^{14}C-leucine 4 h later. After a 1 h labelling period, livers were removed and pooled and the nuclear acidic proteins were prepared by selective extraction of the isolated nuclei in phenol[9]. The mixed proteins from hormone-treated and control animals were co-electrophoresed in 10% polyacrylamide gels containing SDS. The banding pattern was revealed by staining with 'Amidoblack 10B' and the gel was sliced in 1 mm slices. Radioactivity in individual slices was determined by combustion and scintillation spectrometry. The lower curve shows the ratio of ^{3}H/^{14}C incorporation into the acidic proteins at different positions in the gel. The upper curve shows the relationship between electrophoretic mobility and protein molecular weight. Note the increased incorporation of ^{3}H-leucine into proteins of molecular weight 60,000 and 80,000, respectively, in the glucagon-treated rat livers.

To determine whether chromatin composition can also be influenced by peptide hormones, we have investigated the effects of glucagon on the synthesis of different acidic proteins of liver nuclei under conditions in which gene activation for RNA synthesis is known to occur. Gene activation by glucagon is manifest in the *de novo* synthesis of a number of liver enzymes, the induction of which depends on the synthesis of "new" RNA molecules[7,8].

To compare the synthesis of chromosomal proteins in control and hormone-treated animals, pairs of adult, male Sprague–Dawley rats, maintained on 'Purina' chow diet *ad libitum*, were injected intraperitoneally with 400 µg of glucagon in 0.5 ml. of 0.14 M NaCl. Control animals received isotonic saline. After 4 h, the hormone-treated animals were pulse-labelled for 1 h by intraperitoneal injection of 1 mCi of DL-4,5-^{3}H-leucine (specific activity 15 mCi per mmol). Control animals received 200 µCi of uniformly-labelled L-^{14}C-leucine (specific activity 300 µCi per mmol) at the same time.

After the labelling period the animals were killed by cervical dislocation and the livers were removed and pooled before isolation of the acidic chromosomal protein fraction. This procedure ensured that the ^{3}H-labelled proteins from the glucagon-treated animals and the ^{14}C-labelled proteins

from the control animals were exposed to the same conditions throughout the course of their isolation.

The livers were minced and homogenized in 0.32 M sucrose and 3 mM MgCl$_2$ and the nuclei were purified by centrifugation through 2.4 M sucrose and 1 mM MgCl$_2$ as described previously[9]. The isolation of the nuclear acidic proteins was based on their solubility in phenol[1,9] after removal of the saline-soluble proteins in 0.14 M NaCl and extraction of the histones in 0.25 M HCl. The acid-extracted nuclei were treated to remove lipids and subsequently suspended in 0.1 M Tris (HCl), pH 8.4, containing 0.14 M 2-mercaptoethanol and 0.01 M EDTA. The suspension was extracted with phenol and the protein in the phenol phase was subsequently restored to an aqueous phase by a series of dialyses against urea-containing buffers[9]. The acidic chromosomal proteins were finally dialysed against 0.01 M sodium phosphate buffer, pH 7.4, containing 0.14 M 2-mercaptoethanol and 0.1% sodium dodecylsulphate (SDS). Aliquots of this solution containing 250 µg of protein were analysed by electrophoresis in 10% polyacrylamide gels. The electrophoretic separation of the acidic protein–SDS complexes was carried out as described previously[9]. The gels were stained with 'Amidoblack 10B' to reveal the characteristic banding pattern of the liver nuclear phenol-soluble proteins, and cut transversely in 1 mm slices. The radioactivity in each slice was determined by scintillation spectrometry after separation of the ^{3}H-labelled and ^{14}C-labelled combusion products in a 'Packard Tri-Carb Model 305 Sample Oxidizer'.

The results of the double-labelling experiments are summarized in Fig. 1. The electrophoretic pattern contained a series of protein bands, each of which contained a mixture of the ^{3}H-protein from the hormone-stimulated nuclei and the corresponding ^{14}C-protein from the control nuclei. In Fig. 1, the ratio of ^{3}H-activity to ^{14}C-activity is plotted for each of the 1 mm slices cut from the gel. This ratio is an indication of the relative rates of synthesis of individual nuclear proteins derived from the glucagon-treated and control animals. The ^{3}H/^{14}C ratio was remarkably uniform for all proteins in the gel except for two bands located in gel slices 5 and 19. Here the abrupt change in isotope ratio indicated a selective stimulation of synthesis of these particular proteins in the glucagon-treated animals. The relationship between protein mobility and molecular weight is plotted in the uppermost curve of Fig. 1. The molecular weights of the proteins specifically responding to glucagon stimulation were estimated at approximately 60,000 and 80,000 respectively.

It is of interest that no change in isotopic amino-acid ratio was evident in the protein band corresponding to a molecular weight of 41,000 which was shown to be responsive to cortisol stimulation[1]. This is a clear indication of the different modes of action of the steroid and peptide hormones on the nuclei of the same target tissue.

The question arises as to whether the effects of glucagon on the synthesis of liver nuclear proteins are direct, or whether they are mediated through the release of other hormones, such as insulin or pituitary hormones. The effects of insulin were examined in parallel studies in which adult, male rats weighing about 200 g were injected with 1.25 units of insulin, and control rats with saline. Hormone-treated animals were pulse-labelled 4 h later, for 1 h with ^{3}H-leucine, and control animals received ^{14}C-leucine. The livers were pooled, and the nuclear acidic proteins were prepared and analysed by polyacrylamide gel electrophoresis as described. The ^{3}H/^{14}C ratio was determined for each of the mixed protein bands in the gel, and no significant increase in ratio was observed for those protein bands which were most responsive to glucagon administration. This result makes it unlikely that the glucagon effects on nuclear protein metabolism are mediated through the release of insulin.

This is the first indication that peptide hormones such as glucagon can modify the composition of the chromatin by selectively stimulating the synthesis of particular nuclear acidic proteins. There is extensive evidence, however, that cyclic AMP mediates the action of glucagon on the liver[10-12] and that it also has a rapid and selective effect on the phosphorylation of different acidic proteins of the liver nucleus[13].

Administration of glucagon *in vivo* leads to a selective stimulation of synthesis of two acidic proteins in liver cell nuclei, of molecular weight 60,000 and 80,000 daltons, respectively.

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Are African Elephants deficient in Essential Fatty Acids?

THE African elephant (*Loxodonta africana*), living in its natural habitat in East Africa, has suffered over the last few decades from progressive restrictions resulting in overcrowding within national parks and sanctuaries[1,2] and a relatively rapid deterioration of its habitat from woodland to open grassland[3,4]. Much of the latter change has been precipitated by the elephants themselves pushing over young trees to eat the succulent growing shoots, or stripping the oil bark and exposing the trees to damage by periodic fires[5].

Laws[6] described puberty retardation and an extension of the mean calving interval in mature cows in northern Uganda elephant populations. He suggested that these changes were due to inadequate nutrition. Sikes[7] has also suggested the presence of a nutritional stress in grassland elephants. Intake of the essential fatty acids (EFA), linoleic and linolenic, by grassland elephants decreases dramatically during the dry season[8], paralleled by a similar decrease in the growth rate[9]. Wild African buffaloes (*Syncerus caffer*), living in deteriorated habitats similar to those occupied by elephants, have been shown to have lower concentrations of essential fatty acids in their tissues than buffaloes living in more wooded areas of East Africa[10], and a similar pattern of depletion might therefore occur in grassland elephant populations.

I investigated this possible EFA deficiency by analysing the component fatty acids of the lipids extracted from the sera obtained from two adult female non-pregnant lactating elephants, shot in Murchison Falls National Park, Uganda. Serum collection and the mean serum lipid values of these and other elephants have been reported elsewhere[11]. Separation of the major lipid classes was carried out by thin-layer chromatography and the fatty acid methyl esters from each class were prepared by *trans*-methylation[12]. The component fatty acid esters were examined by gas-liquid chromatography, using a flame ionization detector, and two columns of differing polarity (polyethylene glycol adipate on celite at 180°, and 'Apiezon L' on celite at 200°). Peaks were identified by comparison of their log retention times with those of methyl palmitate on both columns, and by comparison with standard mixtures.

Table 1 Fatty Acid Composition (wt. % of Total) of Serum Cholesterol Esters and Triglycerides

| | Cholesterol esters | | Triglycerides | |
Fatty acid	Murchison Falls elephant serum *	Kenya-Uganda elephant serum †	Murchison Falls elephant serum *	Kenya-Uganda elephant serum †
14 : 0	0.4	1.0	3.2	2.6
16 : 0	15.5	14.0	43.1	40.5
16 : 1	5.5	2.8	2.2	2.6
17 : 0	0.4	0.3	0.7	1.4
17 : 0 br	—	0.8	—	1.0
18 : 0	1.8	1.8	8.6	10.2
18 : 1	35.2	21.2	38.8	31.9
18 : 2	29.7	42.4	0.6	5.2
18 : 3	7.6	1.3	2.8	0.2
20 : 3	0.2	5.2	—	0.9
20 : 4	3.7	5.6	—	0.9

* Mean of 2 ♀ elephants from Murchison Falls National Park, South Bank.

† Mean of 2 ♀ and 3 ♂ elephants from Kenya and S.W. Uganda; Moore and Sikes[13].

Table 1 shows the percentage fatty acid composition (by weight) of the serum cholesterol esters and triglycerides. Each figure represents the mean of the two individual samples. Also included in the table for comparison are the values obtained independently by Moore and Sikes[13] for elephants from a different East African population. The cholesterol in the serum of the elephant was predominantly esterified with unsaturated fatty acids, as it is in man[14]. The major saturated fatty acid was palmitic acid (16 : 0), as in man[14], the domestic ox[15], and the rabbit[16]. In these species, the major unsaturated fatty acid in the cholesterol esters is linoleic acid (18 : 2) but in the elephant samples it was oleic acid (18 : 1). This is in contrast to the findings of Moore and Sikes (see Table 1) who found twice as much linoleic acid as oleic acid in the cholesterol esters of elephant plasma, but the animals they studied were from populations which had access to plentiful browse, unlike the animals described here. These investigators also found 5.2% (see Table 1) of an eicosatrienoic acid in the cholesterol esters which they identified as 20 : 3, *n*-6. Neither of the two elephants described here had appreciable amounts of this fatty acid in its serum cholesterol esters.

Table 2 records the fatty acid composition of the serum phospholipids from these elephants. As these animals were both lactating adult females, I have included in the table for comparison the data for serum phosphoglyceride composition for adult women given by Olegard and Svennerholm[17] as well as the additional elephant data of Moore and Sikes[13]. It will be seen that in the elephant the predominant fatty acid was stearic (18 : 0) whereas in women it is palmitic (16 : 0); also both these analyses and those of Moore and Sikes showed considerably less linoleic acid (18 : 2) in the phosphoglycerides of the elephant than in women. As with the cholesterol esters and triglycerides, the elephants described here had a

Table 2 Fatty Acid Composition (wt. % of Total) of Serum Phospholipids from Two African Elephants

| | Phospholipid composition | | |
Fatty acid	Serum from Murchison Falls elephants *	Serum from Kenya-Uganda elephants †	Plasma from post-parturient women ‡
14 : 0	0.2	—	—
16 : 0	13.5	15.4	31.3
16 : 1	0.2	0.9	1.4
17 : 0	0.2	0.8	—
18 : 0	41.7	32.6	11.5
18 : 1	15.5	12.2	14.3
18 : 2	9.1	12.3	22.1
18 : 3	2.0	0.7	1.0
20 : 0	1.1	1.4	—
20 : 2	3.3	1.2	—
20 : 3	4.3	6.2	3.3
20 : 4	4.4	6.3	8.5
22 : 0	4.5	—	—

* Mean of 2 ♀ elephants from Murchison Falls National Park, South Bank.

† Mean of 2 ♀ and 3 ♂ from Kenya and S.W. Uganda; Moore and Sikes[13].

‡ Mean of 20 Swedish women; Olegard and Svennerholm[17].

lower concentration of linoleic acid in the phospholipids than those described by Moore and Sikes.

Appreciable amounts of eicosatrienoic fatty acids were present in the phospholipids of these elephants' serum. There are at least two different eicosatrienoic acids which may occur in serum lipids, one synthesized from oleic acid (18 : 1, *n*–9) in EFA deficient animals[18] and designated 20 : 3 *n*–9, and another which is an intermediate in the synthesis of arachidonic acid (20 : 4, *n*–6) from linoleic acid (18 : 2, *n*–6) and which is designated 20 : 3, *n*–6. The value shown in Table 2 for phospholipid 20 : 3 is a combined figure for total eicosatrienoic acids. A ratio of total eicosatrienoic acid to arachidonic acid in the phospholipids in excess of 0.4 has been shown by Holman[19] to be characteristic of EFA deficiency. While Holman suggests that this ratio should be more precisely stated as 20 : 3, *n*–9/20 : 3, *n*–6, he also suggests that the triene-tetraene ratio is valid in most natural dietary situations in which linoleate is the dominant EFA. I did not separate 20 : 3, *n*–6, from 20 : 3, *n*–9, and therefore cannot state this ratio exactly, but the dominant fatty acid in the dietary lipids of the elephant is certainly linoleate[8] and I feel justified in estimating this ratio from total 20 : 3 and 20 : 4 levels, more especially as there is evidence from recent studies that 20 : 3, *n*–6, is raised as well as 20 : 3, *n*–9, in experimental EFA deficiency[20,21].

The total eicosatrienoic : arachidonic acid ratios in the phospholipids of the two elephants studied here were 0.57 and 1.04 respectively. Both these ratios are in excess of 0.4, which suggests that their dietary intake of EFA was inadequate. This interpretation is strengthened by a re-examination of previous analyses of the diet. These showed that fat represented only 4.6% of the total calorific value of the elephants' diet and that linoleate represented only 4.7–9.5% of the total dietary fatty acids. It can be calculated from these figures that linoleic acid accounted for only 0.2–0.4% of the total dietary calories, well below the 1% level necessary to prevent EFA deficiency in rats, guinea-pigs, swine and man[22].

If EFA deficiency exists in the Murchison Falls elephant population, as this work suggests, it could also exist in other overcrowded populations in East Africa, and thus go a long way towards explaining the remarkable tree damage inflicted by elephants in Serengeti National Park in Tanzania, Tsavo National Park in Kenya, as well as in Murchison Falls National Park. The Terminalia trees in Murchison Falls and Baobab trees (*Adansonia digitata*) in Tsavo are both highly sought after by elephants. The woody pulp and bark from these trees have been found to contain higher concentrations of linoleic acid than other available grazing in these areas

(ref. 8, and unpublished observations). Excessive tree damage by elephants may therefore be a natural response to an inadequate fatty acid intake.

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Lightning as Background Noise for Communication among Electric Fish

An appreciation of the background noise of the communication "channel" is crucial to our understanding of animal communication systems. Lightning[1–4] is one source of naturally-occurring, non-biological electrical noise that is within the frequency range of electric communication by fish (below 20 kHz), and there may be others[5]. It is an important noise source because thunderstorms are especially common over South America and Africa where electric fish are found[6,7], and electromagnetic waves from lightning propagate long distances according to the inverse first power of distance[1]. I investigated the importance of this noise during a field study of gymnotid fishes in Guyana, South America (3° 19′ N; 59° 39′ W).

On June 21, 1971, at 2300, I immersed two small wire electrodes, 30 cm and 50 cm apart, to a depth of 15 cm in a quiet region of a small, freshwater creek. The specific conductance of water was 4.36×10^{-5} mho cm^{-1}. The electrodes were oriented horizontally and were connected by shielded wires to an audio amplifier and tape recorder ('Uher 4400'). The overall frequency response (3 db) of the recording system was from 20 Hz to 18 KHz and the RMS thermal noise of the system with the input shorted was less than 2×10^{-8} V Hz$^{-1/2}$ across the frequency spectrum, significantly less than the signals to be discussed here.

Oscilloscope tracings of recorded electrical activity revealed many brief fluctuations in the electric field of the order of several microvolts per cm. There were often ringing trains of

oscillations typical of the multiple echoes between the Earth and ionosphere (Fig. 1a). Sound spectrograms of recorded activity show "clicks" as events composed of many frequencies of nearly equal intensity, and also "tweeks" as frequency-modulated signals that approach, asymptotically, the Earth-ionosphere cavity or waveguide cutoff frequency of about 2 kHz (Fig. 1b). Both oscilloscope and spectrograph records resemble those of other authors who considered the signals were caused by lightning discharges[2,4,8,9]. Also, visible lightning flashes were accompanied by a sharp "click" on the tape recorder monitor on other occasions.

The amplitude of the electrical noise was analysed with an electronic counter arranged to count events with amplitudes that equalled or exceeded a series of thresholds. The upper frequency limit of the counter was 200 kHz. Data for electrode spacings of 30 cm and 50 cm are shown in Fig. 2. Each point is an average of 60 s of activity. Over the range of field strengths illustrated, the slope of the line varies between -2.27 and -3.85. This curve can be used to estimate the frequency of effective noise that is perceived by an electric fish; however, some measure of threshold is needed.

Most "clicks" were brief, approximately 0.2 ms in duration, as are the return strokes of a lightning discharge[1]. The behavioural threshold of an African electric fish, *Gymnarchus niloticus*, for detection of a single, 0.2 ms rectangular electrical pulse is 18 μV cm^{-1} (ref. 10). This value, indicated on Fig. 2, suggests that *Gymnarchus* should be sensitive to electromagnetic pulses occurring, on average, once every five seconds. Other threshold measurements suggest a more serious consequence of noise. *Gymnarchus* is more sensitive to pulses of longer duration, and the threshold for sensing pulse trains is far less than for single pulses. *Eigenmannia* responds to sinusoidal electrical stimuli near its own frequencies by shifting its discharge frequency away from the stimulus frequency. This response, the Jamming Avoidance Response, has a threshold sensitivity of less than 0.25 μV cm^{-1} (ref. 11). Electric fish can detect electrical noise from lightning and other atmospheric sources but the degree to which this noise interferes with communication remains unknown.
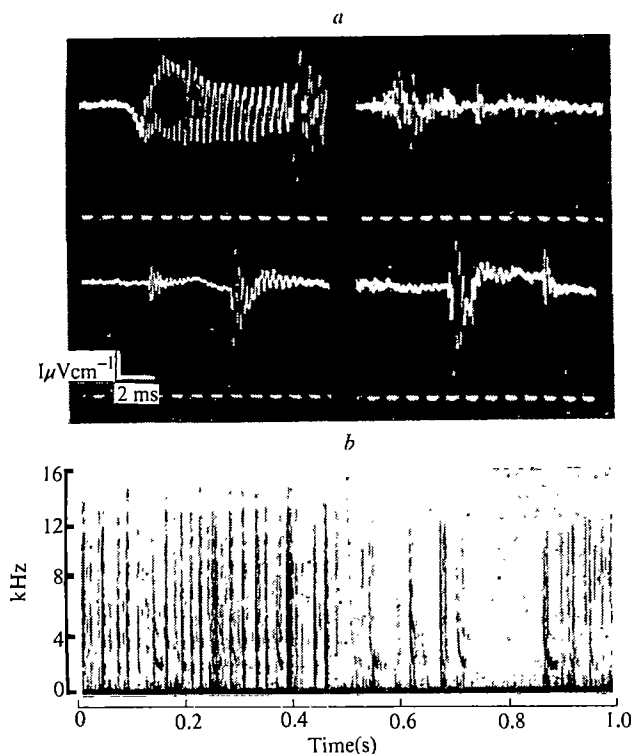
Fig. 2 Amplitude of electrical noise recorded from Moco-moco Creek, June 21, 1971, plotted against the frequency of occurrence of events of the same or greater amplitude. Electrode spacings (O—O) 30 cm and (●—●) 50 cm. The vertical broken line at 18 μV cm^{-1} is the threshold sensitivity of *Gymnarchus niloticus*.

If the social organization of electric fish requires electrical communication at a distance, then natural selection will favour communication signals that contrast with this background noise. Continuous and regular trains of pulses from gymnotid fish both with "tone" and "pulse" electrical emissions[12] contrast with the randomly-occurring lightning noise. The receiver can filter out unwanted frequencies and so increase the signal-to-noise ratio.

Certain species of electric fish such as the electric eel and some mormyrids have discharges that do not contrast with lightning noise. Their discharges, which are possibly used for object location, occur at random intervals at a low frequency. The electric eel is a predator, and to be electrically inconspicuous may be an advantage which enables it to approach prey without being detected. Small gymnotids may be part of its diet. Although mormyrids have brief, erratic discharges that must be difficult to distinguish from lightning, Moller[13] found that *Gnathonemus niger* produced a highly regular discharge in the presence of the discharges from another electric fish; some mormyrids may therefore "regularize" their discharges, so permitting communication at a distance.

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Fig. 1 Examples of naturally-occurring electrical noise recorded from Moco-moco Creek, Guyana, on June 21, 1971, at 2300. *a*, Oscilloscope tracings of noise at electrode spacing of 50 cm. *b*, Sound spectrograph of portion of recording, range 160 Hz to 16,000 Hz; bandwidth = 600 Hz.

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Fig. 1 Schematic diagram of bombardment and counting apparatus. The cyclotron beam was 1 μA of 8 MeV protons. The "rabbit" is shown in both bombard and count positions in the diagram.

Rapid Determination of Very Low Nitrogen Levels in Water

THE importance of nitrogen in the various life cycles of interacting ecosystems has been well described[1-4]. The pertinent concentration levels may be as low as 5×10^{-9} g kg^{-1} in water[3]. Quick, accurate and nondestructive tests for the presence of these levels of nitrogen are of practical importance. We report here a new approach to ^{14}N assay, associated with the evaporated detritus of less than 4 ml. of water. The present overall accuracy is about $\pm 25\%$ at concentrations greater than 200×10^{-9} g kg^{-1}; the test is sensitive down to levels of about 20×10^{-9} g kg^{-1}. These figures can be improved by relatively simple procedures. The testing time per sample is about 3 min and the sample is not destroyed by the test.

In this method, namely charged particle (nuclear) activation analysis (CPAA), the activation (A) and subsequent decay (B) processes are

$$\text{(A)} \quad {}^{14}\text{N} + p \rightarrow {}^{14}\text{O} + n; \quad Q = -5.9 \text{ MeV}$$
$$\text{(B)} \quad {}^{14}\text{O} \rightarrow {}^{14}\text{N} + \gamma + e^+ + \nu; \quad \tau_{1/2} = 71.0 \text{ s}$$
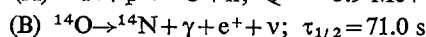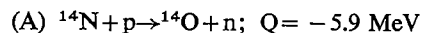
The presence of nitrogen is measured by counting the number of 2.31 MeV gamma rays emitted in reaction (B). The activation is produced by a 1 μA beam of 8 MeV protons from a 76 cm cyclotron and the gamma rays detected with a sodium iodide scintillator following rapid transfer of the target to the counting location. After 5–10 min of decay the sample can be retested. In general, chemical tests are both highly specific and destructive; that is, they test for only one element (or even one compound of that element) and destroy or alter the sample during the test[5]. Also most chemical tests for total nitrogen detect the presence of dissolved gaseous nitrogen along with the other chemical forms of nitrogen. Our method is insensitive to volatilized nitrogen. All these differences tend to make the approaches of chemical analysis and CPAA complementary techniques.

Initial applications of the method have been made on water samples from Lake Tahoe, the Sacramento River, municipal wells, and public drinking fountains. We found that with a few simple improvements the method could be utilized to monitor a few hundred samples a day at levels greater than about 10×10^{-9} g kg^{-1}.

The method of bombardment, detection, and counting is shown schematically in Fig. 1. A 9.1 m pneumatic tube, the "rabbit tube", carried the target between the bombard and count positions with a transit time of less than 2 s. Each target was a 1.59 cm diameter tantalum foil, 0.006 mm thick with a 5 mm diameter and an indentation 1 mm deep in which the water sample was evaporated. A master timing control chassis opened and closed a shutter allowing the 8 MeV beam of protons to pass through a thin Ni foil onto the Ta target foil for a precise time. The foil was, of course, positioned in the same way from one bombardment to another. Calibration foils were interlaced with all unknown runs and the total amount of charge was recorded and used as a relative basis of comparison. The degree of self-consistency of this calibration technique determined our ultimate accuracy ($\pm 25\%$). The overall cycle was 60 s bombard, 30 s wait, 80 s count. Further details can be found elsewhere[6].
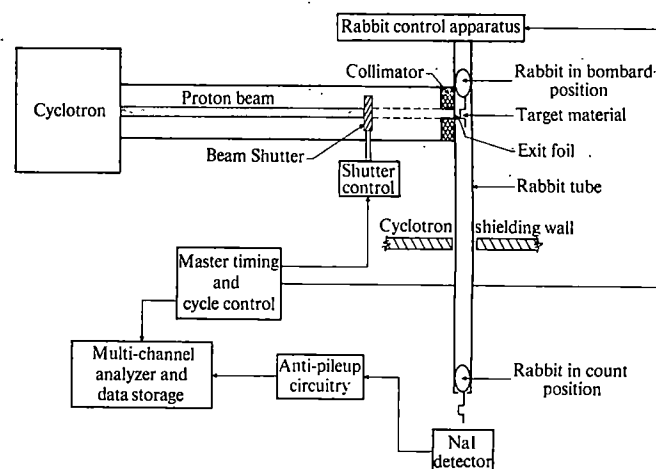
The detector assembly consisted of a 12.7 cm diameter by 20.3 cm long NaI(Tl) crystal mounted on a photomultiplier tube. The pulses from each event in the scintillator were stored in a multichannel analyser as counts versus pulse amplitude. Except for one sample, which showed a peak at 2.1 MeV from activation of sulphur with a 32 min half-life, the ^{14}O decays provided the only peak in the spectrum above 1.3 MeV. The spectrum at lower energies was dominated by an intense peak at 0.511 MeV from positron annihilation following competing reactions. This potential source of electronic pile-up background was eliminated by anti-pile-up circuitry[7] allowing detection of the desired gamma rays in the presence of counting rates up to 10^5 s^{-1} below 1 MeV. The remaining smooth background under the peak of interest was due to electron bremsstrahlung and was easily subtracted.

Our calibration standards were prepared from water solutions with known amounts of (dissolved) AgNO$_3$. The calibration results are shown in Fig. 2. The scatter in the two sets of results shown is due mainly to two factors: (1) the variable amount of background nitrogen adsorbed onto the tantalum backing; for our experimental conditions this leads to a lower limit of about 20×10^{-9} g kg^{-1} for the lowest level of detectability; (2) the clumping of the solid residue of evaporation at levels greater than 100×10^{-9} g kg^{-1} which caused a $\pm 25\%$ scatter in the experimental results. The first problem may be ameliorated by the use of different backings, but to solve the second problem requires a somewhat more sophisticated evaporation technique than we used. Such a technique has already been used successfully for CPAA[8] for far more heavily loaded water solutions than we used. The final result for our calibration curve is

$$10^{-9} \text{ g kg}^{-1} \text{ by weight of nitrogen} =$$
$$\{[6.1 \pm 0.2] \text{ counts } \mu\text{C}^{-1} - [32.5 \pm 8.0]\} \times 10^{-3}$$

The errors pertain strictly to the particular count cycle and sample size given above, and can of course be reduced by repeating the run an appropriate number of times but this constitutes no improvement in the method.

Table 1 gives the results of our method when applied to six different water sources, all from Northern California except for one sample from Colorado. The sensitivity of the method is also seen from the fact that the detection of approximately 20×10^{-9} g kg^{-1} nitrogen in water requires an actual deposition on the target foil of about 80 ng of nitrogen.

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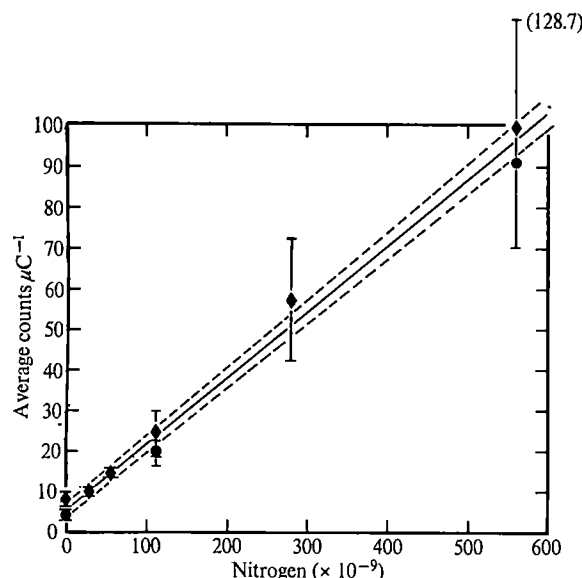
Fig. 2 Calibration curve for count/bombard cycle and beam conditions described in the text. Two sets of experimental results, shown by the two different symbols, are shown to demonstrate variability due to fluctuation in adsorbed nitrogen at low levels (less than 40×10^{-9} g kg^{-1}) and irregularities in sample preparation at high levels (greater than 100×10^{-9} g kg^{-1}). ——, Plot derived statistically using all the data; - - -, present error limits.

It is not surprising to find that the Lake Tahoe sample has the lowest value of nitrogen contamination in the table, as it is a good example of an oligotrophic lake[3], that is, very low in organic growth. Samples 2 and 3 (Table 1) are from different sources at the University of California, Davis, where the water distribution system has not undergone any major change for the past few years. Accordingly it is felt that the change in nitrogen level in sample 3 for the two dates, one year apart, is very probably due to a change in the well-sources feeding the university system. This is supported by sample 4, where we see the widely divergent results of three different well sources from the city of Davis water supply system. Well No. 18 is a new, 1972, well, and an independent chemical test (D. Pelz, Public Works Director, Davis, private communication) for NO$_3$ (nitrate) in the water from this well and Well No. 10 gave results of 3,160 and 925×10^{-9} g kg^{-1} respectively (error about $\pm 10\%$ in both cases) of nitrogen in this form. As these figures agree reasonably well with our results for total nitrogen we suggest that most or all of the nitrogen is in the NO$_3$ form in both wells. Neither figure approaches the present US Public Health Service limit of acceptability, which is $10,000 \times 10^{-9}$ g kg^{-1}. Another conclusion from the comparison of our results and those of the chemical analysis is that the loss of nitrogen during evaporation is not likely to originate from the nitrate form.

Our results represent only preliminary indications of the

Table 1 Application of Nitrogen-Activation Method to Various Water Sources

Sample origin	Date	g kg^{-1} $\times 10^{-9}$
1. Lake Tahoe, California; supplied Dept. of Zoology, Univ. of Calif., Davis	March 1972	21± 16
2. Tapwater, Environmental Eng. Lab., Univ. of Calif., Davis	14/6/71	45± 31
3. Drinking water, Walker Hall, Univ. of Calif., Davis	14/6/71 4/ 7/72	80± 42 340±110
4. City of Davis, California Well number 10 Well number 17 Well number 18	7/ 6/72 7/ 6/72 7/ 6/72	755± 35 180± 45 2,835±266
5. Sacramento River, Three-Mile Slough	April 1972	83± 43
6. Colorado River, below Lake Havasu	23/3/71	400± 80

potential of our approach to the problem of low-level nitrogen monitoring. Two important but simple improvements have already been mentioned, and with these the accuracy at higher concentrations would be essentially unlimited (except for the pile-up effects already mentioned) and the lower limit of sensitivity would be about halved. The relatively modest accelerator requirement, that is, an 8 MeV proton beam of about 1 μA, makes the method universally applicable.

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Odour-Blindness to Musk: Simple Recessive Inheritance

Three types of odour-blindness or specific anosmia have been studied, but genetical evidence so far obtained is tentative or inconsistent[1]. The rare anosmia to the n-butyl-mercaptan of skunk[2], and more commonly the scent of freesia flowers[3], may be inherited as autosomal recessive traits. Anosmia to hydrogen cyanide[4-6] is complex and its inheritance has not been confirmed[7].

Specific anosmia to the musk pentadecalactone[8] (Thibetolide^R, Givaudan Corp., New Jersey) was found in about 7% of tested subjects. The individual odour detection thresholds for ninety subjects tested with a dilution series are shown in Fig. 1. The saturated solution (dilution 0) 1.1 p.p.m., w/v, was prepared by shaking 1.1 mg of pentadecalactone in 1 l. of water after warming to 40° C to melt the musk and binary dilutions made from this. The test procedure and necessary precautions have been described[9,10]. The majority of subjects (eighty-four) had thresholds forming a roughly Gaussian curve between dilutions six and fourteen, having a mean normal detection threshold of 10.1 dilution steps (exactly 1 part of musk in 10^9 of water), and standard deviation ± 1.48 steps. A minority of six subjects (6.7%) had thresholds at higher concentrations, and one could not smell the saturated solution. To make an arbitrary distinction between normal observers and specific anosmics, we used step 6.5 on Fig. 1 (0.0123 p.p.m. pentadecalactone in water) which represents twice the average standard deviation for 18 other odorants[9].

Anosmia to the sweaty odour of isovaleric acid affects about 2% of the population[11]. The corresponding diagnostic strength for purified[9] isovaleric acid is 2.35 p.p.m. in 0.01 N H$_2$SO$_4$. As a control we used 41.1 p.p.m. purified isobutyl isobutyrate. This complex fruity odour screened out any general anosmics having little or no sense of smell (about 0.2% of the population[2]).
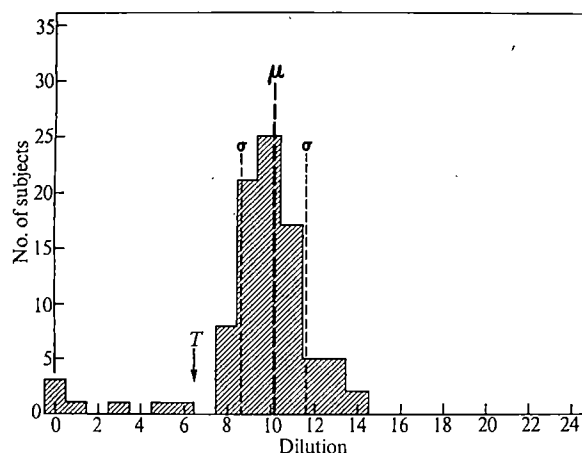
Fig. 1 Olfactory thresholds of ninety persons to pentadecalactone dilutions in water. μ, Mean normal threshold; σ, standard deviation; T, test concentration for distinguishing specific anosmics.

Our modified test procedure was conducted in an odour-free environment. The subject received a tray with 3 glass-stoppered 125 ml. Erlenmeyer flasks, one containing 20 ml. of odorous solution and the other two odourless water in a double-blind trial. The trays were presented to the subjects in the sequence: isobutyl isobutyrate, isovaleric acid, pentadecalactone, and the flask with odour selected by sniffing. When a decision was recorded for each tray, the flasks are randomized again and the series repeated. A subject was scored as a non-smeller of the test compound if he failed on either trial. Odorous flasks were used for not more than 10 subjects before replacing the solution. The subjects did not wear perfume, and refrained from eating, drinking or smoking for 15 min before the test, as these factors temporarily decrease olfactory sensitivity[9]. Any kind of nasal pathology such as colds, allergies or sinusitis may cause a loss of sensitivity[12] averaging 2 dilution steps[9].

We present results on 109 Caucasian families in whom all known inherent and environmental interferences with olfactory sensitivity have been excluded. Although adult olfactory acuity decreases somewhat with age[13], there was no significant difference in the incidence of anosmia to isovaleric acid or pentadecalactone between the 218 parents (average age 41.2) and 266 children (5 to 18 years, average 12.1). None of the 484 subjects failed to smell isobutyl isobutyrate, 6 (1.2%) failed isovaleric acid, and 42 (8.7%) failed musk, frequencies agreeing with those reported earlier[8,11] and shown in Fig. 1.

The isovaleric acid data implied recessive inheritance but were too meagre for analysis. Insensitivity to musk occurred in thirty-six families (Fig. 2); males and females were equally affected. The offspring from twenty marriages between smellers were analysed by the a priori method[14] (Table 1), and there was almost exact correspondence between the expected and observed results.

Among the fifteen marriages between smeller and non-smeller, thirteen produced only smeller children, probably because of small family size. Two marriages produced a total of three children, one smeller and two non-smellers. A marriage between non-smellers produced two children, both non-smellers.

The data acquired with this test protocol, though not conclusively ruling out polygenic inheritance[14,15], strongly suggest that the inability to smell pentadecalactone is inherited as a simple recessive autosomal character. The high incidence of the anosmia suggests a genetic polymorphism, but might result from relaxation of natural selection on the human olfactory sense.

There was no evidence of non-random mating or selection for this trait, so that the observed recessive proportions from

Table 1 Segregation Analysis of the 20 Families with Normal Parents and at Least One Affected Child (a priori Method)

Size of sibship (n)	No. of sibships (x)	$q'n$*	Total affected Expected $q'nx$	Observed
1	2	1.000	2.000	2
2	5	1.143	5.715	7
3	8	1.297	10.376	11
4	1	1.463	1.463	1
5	2	1.640	3.280	2
6	2	1.825	3.650	2
	20 †		26.484	25

$$* q' = \frac{1/4}{1-(3/4)^n}$$

† Total: 62 children.

the various marriage types should fit those expected for a population in equilibrium with $q=0.2945$. This was not true. Scrutiny of the data revealed two groups distinguishable by national origin. In fifty-five families the parents were at least third generation Americans of Western European descent. In fifty-four families the parents had migrated after the Second World War from Western Europe or had immigrated from outside Western Europe. In the first group ($q=0.2577$) gene frequency analysis showed agreement between observed and expected results, but in the second group ($q=0.3270$) it did not. We attribute these results to the different degrees of national homogeneity discernible in the family histories.

We have found significant differences in the frequencies of specific anosmias between two human races. Isovaleric acid anosmia is prevalent (9.1%) among our sample of seventy-seven Negroes and uncommon (1.4%) in our sample
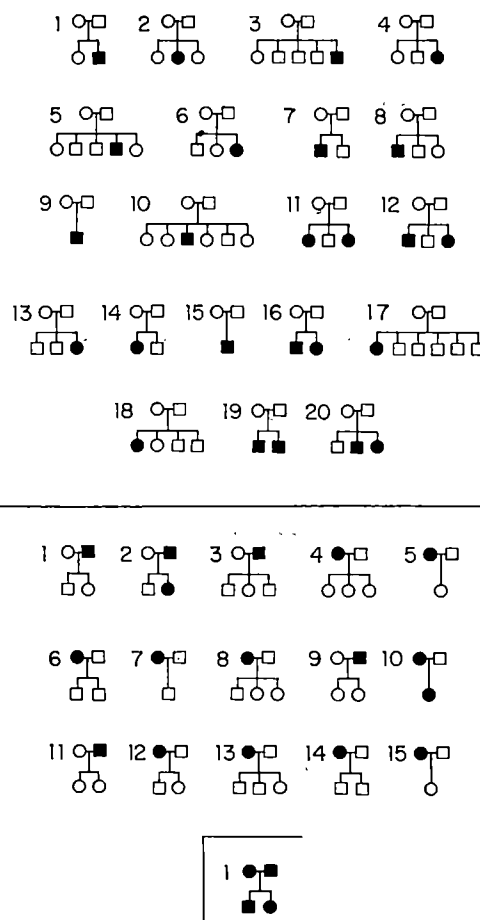
Fig. 2 Family trees showing the occurrence of odour-blindness to pentadecalactone (solid symbols).

of 849 Caucasians. Musk anosmia occurred in 7.2% of the Caucasians but in none of the Negroes. We suspect wide variations in the incidence of specific anosmias within races.

The origin for specific anosmia could be a defect in the hypothetical olfactory receptor protein, representing one of the physiological primary odours (such as sweaty, musky)[10,16]. An essential corollary of the hypothesis is the demonstrated simple recessive inheritance of specific anosmia, which is only expected if the test odorant is very close to a pure primary odour.

The chemical mapping of specific anosmias is the most logical and practical approach to classifying the primary odours in the human sense of smell[10,11,17]. We think that the study of genetics of the twenty-seven known discrete anosmias[8] would provide many new and accessible polymorphisms for the study of human genetic variation[15].

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Chlordimeform: a Pesticide Acting upon Amine Regulatory Mechanisms

CHLORDIMEFORM (also known as chlorphenamidine or Galecron) is a relatively new acaricide-insecticide of which the mode of action has not been elucidated. It is an economically important pesticide[1,2] and is also an interesting compound from a toxicological point of view, as it is effective against many organophosphate and carbamate resistant pests[3], and causes distinctly different symptoms in insects from conventional insecticides. In addition, it is of pharmacological interest because it belongs to a novel group of insecticides which possess a formamidine moiety.

We have observed that chlordimeform at a high dose (200 mg kg^{-1} injected intraperitoneally (i.p.) approximately LD$_{90}$) causes marked hyperexcitation in a short time period (5 to 10 min) in rats and mice. They exhibit tremors and become extremely hypersensitive to external stimuli. The poisoned

Table 1 MAO Inhibition* by Chlordimeform Analogues and by Known MAO Inhibitors

Structure	pI_{50}*	Name
$\langle\hexagon\rangle$—CH$_2$—CH$_2$—NH—NH$_2$	5.46±0.14	Phenelzine
N$\langle\hexagon\rangle$—C(=O)—NH—NH—CH(CH$_3$)(CH$_3$)	3.50±0.08	Iproniazid
Cl$\langle\hexagon\rangle$(CH$_3$)—N=CH—N(CH$_3$)(CH$_3$)	4.49±0.05	Chlordimeform
Cl$\langle\hexagon\rangle$(CH$_3$)—N=CH—NH—CH$_3$	4.60±0.05	C-8520
CH$_3$$\langle\hexagon\rangle$(CH$_3$)—N=CH—N(CH$_3$)(CH$_3$)	3.85±0.03	
Cl$\langle\hexagon\rangle$—N=CH—N(CH$_3$)(CH$_3$)	3.81±0.07	C-4789
$\langle\hexagon\rangle$—N=CH—N(CH$_3$)(CH$_3$)	3.23±0.01	

* Data expressed as pI_{50}±standard deviation where pI_{50} = $-\log I_{50}$, I_{50}=inhibitor concentration in mol l.$^{-1}$ (final concentration) giving 50% inhibition. Each value is mean of 3–5 determinations. Inhibitors were added to reaction tubes in 20 µl. solvent (H$_2$O or 95% ethanol), Control tubes received solvent alone. Preincubation was begun by addition of enzyme (0.1 ml. of filtered liver homogenate). The reaction was initiated by addition of 0.3 µmol of the substrate kynuramine dihydrobromide in 20 µl. of H$_2$O.

animals show signs of locomotive difficulties partly due to frequent hyperextension of hind legs at later stages.

In sublethal doses (50–200 mg kg^{-1} i.p.) chlordimeform has a sedative effect. The poisoned animals, when placed in an open area, stay motionless in a characteristic low posture unless they are externally stimulated. In rats at all doses tested (50–200 mg kg^{-1}) gradual dilation of pupils took place over a 1 h period. In no cases did the animals show such cholinomimetic symptoms as slowing of heart beat, salivation, urination, or fasciculation, which agrees with the *in vitro* observation that chlordimeform is not an inhibitor of housefly head cholinesterase. Rather, the overall symptoms of chlordimeform poisoning are sympathomimetic in nature.

To study the biochemical cause of chlordimeform poisoning, we have examined its effect upon the monoamine oxidase[4] of the rat liver. Livers were homogenized in 5 volumes of cold distilled water. The homogenate was filtered through glass wool and used directly as the enzyme source. Enzyme and inhibitors were preincubated for 15 min at room temperature. Enzyme activity was defined as the amount of kynuramine metabolized in 20 min at 37° C.

The results (Table 1) clearly indicate that chlordimeform is an inhibitor of monoamine oxidase (MAO). Also, the degrees of inhibitory potency of the chlordimeform analogues are roughly correlated with those of the general *in vivo* toxicity of these compounds[5] to mites. It is expected that some biogenic amines accumulate as a result of monoamine oxidase inhibition *in vivo*. To examine this possibility male rats were treated with 200 mg kg^{-1} (intraperitoneal injection) of chlordimeform. The animals were killed after 1 h and the serotonin and norepinephrine levels in the whole brain were determined by the method of Maickel *et al.*[6]. It was found (Table 2) that the levels of serotonin and norepinephrine in the treated animals were 70% and 22% higher than in control animals.

It is premature to conclude that this inhibitory property of chlordimeform is the sole mechanism by which it poisons the animal. At least some of the symptoms observed during chlordimeform poisoning, however, can be attributed to the

Table 2 Serotonin and Norepinephrine Levels* in Whole Rat Brain

	Chlordimeform	Control
Serotonin	0.75 ± 0.07	0.44 ± 0.06
Norepinephrine	0.22 ± 0.01	0.18 ± 0.03

* Data expressed as $\mu g \ g^{-1}$ wet weight $\pm$ standard deviation. Averages of six animals each for serotonin and three animals each for norepinphrine. Data uncorrected for extraction efficiencies. Male 150 g rats were used. Animals were injected intraperitoneally with 200 mg kg^{-1} of chlordimeform (hydrochloride salt) in aqueous solution, injection volume$=0.7$ ml. Control rats received 0.7 ml. H_2O. Animals were sacrificed 1 h after injection.

accumulation of amines. The overall description of serotonin poisoning[7] in the presence of a monoamine oxidase inhibitor closely resembles that for chlordimeform, and chlordimeform (50 mg kg^{-1} rat, i.p.) antagonizes certain of the symptoms of reserpine intoxication (such as tremors and closed eyelids, with a reserpine dose of 10 mg kg^{-1}).

Another possibility is that chlordimeform can directly react with the receptors for the amines. As these two reactions (MAO inhibition and direct action) could elicit similar poisoning symptoms, we cannot eliminate the possibility at this stage that the latter mechanism could also play an important role in the poisoning process.

Our finding that an insecticidal compound can interfere with amine regulation in animals is entirely new. It is significant in view of the preliminary evidence that chlordimeform does not interact with any other well established biochemical target systems that are known to be related to insecticidal action. A new class of insecticide, acaricides, which act on a different pharmacological principle is important in the light of the urgent need to develop good substitutes for environmentally hazardous pesticides.

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Use of Male Sterilization Mutations for Insect Control Programmes

RESISTANCE and deleterious environmental side-effects have limited the use of insecticides in insect control programmes, and researchers have become increasingly aware of the potential of population control by genetic manipulation. In pioneering experiments, screw-worm fly eradication was accomplished by the release of sterile males into natural populations, and wide use of this method was anticipated[1]. Serious drawbacks, however, have often limited the successful utilization of this approach[2]. Males are usually sterilized by the induction of dominant lethal mutations in a high proportion of sperm and

Treated $X/Y\male \times X^{\text{balancer}}/X^{\text{balancer}} \female$

Single $X^{\text{treated}}/X^{\text{balancer}} \female \times X^{\text{balancer}}/Y\male$

$X^{\text{treated}}/Y\male \quad X^{\text{balancer}}/Y\male \quad X^{\text{balancer}}/X^{\text{treated}} \female \quad X^{\text{balancer}}/X^{\text{balancer}} \female$

Test for fertility | Cross to maintain a male-sterilizing mutation
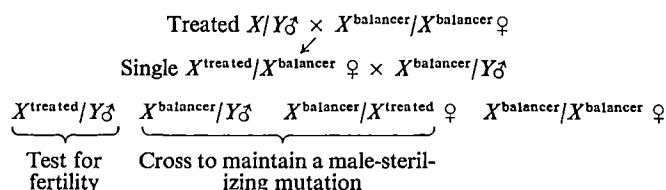
Fig. 1 A scheme to isolate sex-linked male-sterilizing mutations. X^{balancer} indicates an X-chromosome that suppresses recombination and bears a mutation with a visible phenotype.

spermatids by treatment with ionizing radiation or chemical mutagens. In some species the treated males do not compete successfully with males from the natural population for mating partners; in others the sterile males may not trigger a monogamous response in mated females, or male fertility is regained with time.

Release of insects which will have a detrimental impact on natural populations based on other mechanisms has been suggested, including cytoplasmic incompatibility, hybrid sterility, meiotic drive, distorted sex ratios, and conditional lethal factors[3]. Release of translocation- and compound chromosome-bearing insects has been advocated, and there are programmes to recover and characterize translocations for a number of species[4,5].

I suggest that the release of males bearing sterilizing mutations could avoid some of the current drawbacks of induced male sterilization for some insect species. In species with an X/Y system of sex determination, such mutations are easily generated by recovering mutagenized X-chromosomes in females and screening their sons for fertility (see Fig. 1). The mutagenized X-chromosome is recovered heterozygous with an X (denoted "balancer") which has one or more inversions to inhibit recombination and a mutation with a visible phenotype.

I collaborated with Drs D. L. Lindsley and E. Lifschytz in an experiment to generate sex-linked male-sterilizing mutations in *Drosophila melanogaster* by this method. Males were treated with ethyl methanesulphonate at a dose which produced sex-linked lethal mutations on 36.5% of the chromosomes tested. Among the lethal-free X-chromosomes, 4.7% carried an induced male-sterilizing mutation. The nature of the sterile syndrome has been preliminarily characterized for 192 independently generated mutations, and a large proportion are associated with aberrancies of spermatogenesis such that mature, motile sperm are not produced. Twelve mutations which allow males to produce motile sperm have been more extensively characterized (R. E. Denell and M. C. Lim, unpublished results). Males bearing two of these mutations do not copulate; males bearing four mutations have low numbers of weakly motile sperm in the seminal receptacle, but their ejaculate is aspermic; males hemizygous for three other mutations transfer sperm to females, but the sperm are incapable of reaching the female sperm storage organs. Finally, three mutations allow males to produce apparently fully motile sperm which are transferred to females, stored, and disappear from the storage organs at about the same rate as normal sperm. Examination of the eggs laid by such females shows that sperm have not entered them, and an abnormality of the sperm acrosome is implied.

Male-sterilizing mutations have also been induced in *Drosophila* by ionizing radiation, and isolated from natural populations[6]. If *Drosophila* is regarded as a model insect system, male-sterilizing mutations should be easily generated in other species. Eliminating the relatively rare class of mutation which affects mating ability directly, sterile males should be as sexually competitive as any laboratory raised strain. (It would be best to use low mutagen doses to minimize the induction of linked detrimental mutations, although detrimentals could be removed by recombination.) Sterility is immediate and (with the exception noted below) permanent. A preliminary characterization of mutations should allow the choice of one which causes monogamous females to reject further suitors. For

polygamous insects, the choice of sterile males with actively motile sperm should allow these gametes to compete effectively with normal sperm for storage and fertilization.

In the experiment described above, fertility was initially assayed at 27° C. Later retests of males developing at 19° C showed that about one-third of these mutations are temperature-sensitive, and males are fertile. Smith[7] has discussed the release of insects bearing temperature-sensitive lethal mutations for control programmes. If a useful temperature-sensitive male-sterilizing mutation is isolated, a homozygous stock could be expanded to large numbers at a temperature allowing fertility. Culturing an additional generation at a sterilizing temperature and separation of the sexes would provide sterile males for release. Care must be taken, however, that males bearing the mutation will not regain fertility under temperature conditions occurring in the wild. Also, some stocks of temperature-sensitive male-sterilizing mutations appear to accumulate genetic modifiers with time, so that males become fertile at temperatures which formerly sterilized them. Thus any mutant being considered for release must be carefully characterized.

A conventional male-sterilizing mutation could also be utilized for release. In the scheme in Fig. 1, a balancer X-chromosome is used. A balancer could be induced by ionizing radiation or chemical mutagens which cause chromosomal rearrangements, and could be screened by testing for crossover suppression of sex-linked genes, and/or by polytene or meiotic chromosome analysis if they are possible. A balancer is crucial for the rearing of large numbers of sterile males. This would be greatly aided by the induction of a female-sterilizing mutation on the balancer; such mutations are also easily induced in *Drosophila*[6]. Thus a "balanced stock" can be established by crossing Xbalancer ♀-sterile/Y males to Xbalancer ♀-sterile/X♂-sterile females. Among the progeny of this cross, only the parental genotypes are fertile, and (with appropriate monitoring for rare events that cause the system to break down) the stock could be expanded to produce vast numbers of sterile males.

A further sophistication would be the induction of some mutation to facilitate mass isolation of sterile males. Such a mutation should be carried by the balancer chromosome so that sterile males remain maximally vigorous, and should be dominant. Temperature-sensitive dominant lethal mutations or behavioural mutations affecting geotactic or phototactic response or causing paralysis should be useful in this context.

My discussion has dealt with the induction of X-linked sterilizing mutations in species with a heterochromatic Y-chromosome, but the basic concepts are easily applied to species with other sex chromosome systems or for autosomal male-sterilizing mutations, and only small procedural changes are necessary.

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Intra-population Differentiation of Physiological Response to Flooding in a Population of *Veronica peregrina* L.

WHEN a plant population grows in a patchy environment, it can be exposed to a variety of selective pressures. If the resulting disruptive selection is strong enough, intra-population differentiation can occur over distances of a few metres, in spite of the absence of any barriers to gene flow[1,2]. We wish to report an example of such differentiation within a population of the annual forb *Veronica peregrina* L.: the differentiation is with respect to physiological responses to varying régimes of soil moisture.

V. peregrina is apparently a native of the Western Hemisphere, including California, and grows in moist to wet habitats[3,4]. The population studied grows within and around the periphery of a temporary pool in Solano County, California. The pool is about 35 cm deep at its deepest spot and measures about 4 by 10 m. It is filled by seasonal rains which fall approximately from December to March and trigger the onset of germination of *V. peregrina* seed. Seed in the deepest part of the pool, near the centre, germinate under water and give rise to individuals which can be under water or in water-logged soils for 2 months or more. Conversely, individuals arising from seed at the periphery of this pool are seldom under water or in water-logged soil except for short periods after heavy rains. Thus different portions of the population are exposed to very different regimes of soil saturation.

When plants grow in saturated soil, their roots are in oxygen-limiting or anaerobic conditions. Previous work suggests that plant species will have very different physiological responses to such conditions, depending on whether they are, by nature, intolerant or tolerant of flooding[5-7]. In species intolerant of flooding, the oxygen-limiting conditions cause an acceleration of glycolysis and a subsequent accumulation of acetaldehyde and ethanol which have injurious effects on the plants. Furthermore, a "malic" enzyme decarboxylates the malate present to pyruvate, contributing further to ethanol production. In tolerant species, there is no acceleration of glycolysis, "malic" enzyme is not found, and non-toxic malate is the end product of anaerobic respiration[7]. Our principal aim was to see whether such differences in malate accumulation could be found within a population by comparing individuals from the centre with others from the periphery. It should be stressed that the opportunity for genetic exchange by means of seed and pollen between centre and periphery is apparently present because the population is continuous and seed is scattered from the seed capsules which burst open at maturity. Furthermore, though this species is predominantly self-pollinated, some cross-pollination may occur because the flowers are proto-gynous[8] and have some insect visitors[8,9].

Ten families originating from the centre were compared with ten families originating from the periphery. In all cases, a family was made up of individuals grown from seed collected from one mature plant in the field. Two sets of twenty-five seeds per family were germinated on wet soil with one set of one family per pot. The plants were allowed to grow for about 30 days at which time they were 2-5 cm tall and had roots reaching the bottom of the 9 cm-high pots. Then one set of all twenty families was placed in deep metal trays which were filled with water. The water level was kept about 1 cm above soil level at all times, so that the soil was saturated. The second set was kept in flats and was watered daily but excess water drained off freely. Both sets of families were maintained at the experimental regimes for 4 weeks, and then assayed for malate contents. To run the assay, roots were collected and thoroughly washed in running water to rid them of any pieces of extraneous organic material. For each family, the roots were prepared according to the method outlined by Bergmeyer[10]. The malic acid contents were assayed using a modification of the enzymatic method outlined by Bergmeyer[10].

To determine the amount of malic acid in each experimental tube, these tubes were compared visually to a set of standards prepared by serial dilution and containing known quantities of malate. All experimental tubes and standards contained equal volumes of solution. We were primarily interested in a precise comparison of performances of families from the centre versus those from the periphery. Consequently, pairs of families, one from the centre and one from the periphery, were kept adjacent to one another throughout the experiment. The results were analysed using the Wilcoxon signed-ranks test which is most appropriate for paired comparisons.

Table 1 Malate Contents (μg/ml. of Root Extract) of Roots of Centre Families (C) and Periphery Families (P) Grown in Moist and Wet Soil

Pair	Soil conditions				Reaction to increased moisture *	
	Moist		Wet			
	C	P	C	P	C	P
1	0.40	0.65	1.20	0.15	+	−
2	0.40	0.65	9.60	0.15	+	−
3	0.40	0.65	4.80	2.40	+	+
4	0.40	0.65	2.40	1.20	+	+
5	0.40	0.65	1.20	9.60	+	+
6	0.40	0.65	1.20	1.20	+	+
7	0.40	0.65	2.40	0.60	+	−
8	0.65	0.40	1.20	0.60	+	+
9	0.40	<0.01	4.80	0.30	+	+
10	0.05	0.40	13.00	0.15	+	−
X̄	0.39	0.53	4.18	1.62	+	+
Stat. signif.	NS		$P<0.025$		$P<0.001$	NS

* This column represents the change in malate contents as soil moisture is increased.

Table 1 shows the malate contents in roots of all families in moist and wet conditions. In moist conditions, roots of families from the periphery contain slightly more malate than roots of families from the centre, but the difference is not statistically significant. In family pairs grown in saturated soil, however, there is a much greater accumulation of malate in the roots of centre families. This difference is statistically significant. A summary of the reaction to an increase in soil moisture and concomitant decrease in soil oxygen is provided in the third column of Table 1. In all ten families from the centre, there was a sizable increase of malate accumulation. The response is statistically highly significant. In periphery families, there was an increase in six families and a decrease in four families. The average response was an increase which is not statistically significant.

The significant difference in the response to flooding of centre and periphery plants can be understood in terms of the difference in habitats occupied by those plants. Four families from the periphery where soils are seldom saturated showed a decrease in malate contents which may be due to the triggering of "malic" enzyme activity[7]. Six families from the periphery showed some increase in malate contents suggesting they are at least somewhat adapted to flooded conditions. In all families from the centre where flooding is commonplace, the response was a significant increase in malate contents and this increase was significantly larger than the increase in periphery families. Intra-population differentiation for several other characteristics has also been observed within the *V. peregrina* population studied[9]. The distance between the centre and periphery of this population is 2–5 m depending on the location, and the observations reported suggest that differentiation, perhaps produced by disruptive selection, can be maintained over such short distances.

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Pollution of Beaches: Reply to Regnier and Park

Regnier and Park[1] do not appear fully to have appreciated the significant point that emerged from my finding[2] that much higher concentrations of antibiotic-resistant and sensitive coliform organisms were present in specimens of water taken from rivers flowing through urban areas than were present in similar specimens taken from rivers flowing through rural areas. This is that human beings were the main source of the sewage pollution of the rivers and that domestic animals were a comparatively unimportant source. The fact that one cannot differentiate the two kinds of specimens from each other by reference to the ratio of the numbers of resistant and sensitive organisms they contain is therefore irrelevant.

Because of my observations on river waters, domestic animal sewage was not thought to be worthy of consideration as a major source of the pollution I found during my later observations on coastal bathing waters[3]. Also, there have been several reports, including the one referred to in my paper[4], implicating human sewage in this respect and, as one would expect, there was no evidence of any farm waste being drained into the beaches I examined.

My comment that the finding of R+ *Escherichia coli* in sea water provides "stronger evidence of contamination with human sewage", to which Regnier and Park specifically refer, was not made in reference to the possible implication of domestic animal sewage but in reference to the possible implication of excreta from marine life and wild birds—this is clearly stated in my paper.

In view of the many reports of European beaches being closed because of human sewage pollution and even of people being fined for bathing in them, I am surprised that Regnier and Park adopt what, to me, seems a rather complacent attitude to the state of our beaches. I cannot share their view. Although I would not class most of the ones I examined as grossly polluted, some of them, Penarth and Ogmore for example, must have been getting near to qualifying for that definition.

Finally, with regard to the public health aspect, I feel that hygienic principles can mean very little if they condone the immersion of the human body in what are really suspensions of human faeces.

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BOOK REVIEWS

Ecology of the Waters

Marine Ecology: a Comprehensive, Integrated Treatise on Life in Oceans and Coastal Waters. Edited by Otto Kinne. Vol. 1. *Environmental Factors,* Part 3. Pp. ix+1245–1774. (John Wiley: New York and London, February 1972.) £12.
The Estuarine Environment. Edited by R. S. K. Barnes and J. Green. Pp. xii+133. (Applied Science: London, 1972.) £3.50.
Coastal Zone Management: Multiple Use with Conservation. Edited by J. F. Peel Brahtz. Pp. xii+352. (John Wiley: New York and London, March 1972.) £7.65.

In 1972, a year marked by the centenary of the Challenger Expedition and a vocal concern for the state of the global environment, it seemed appropriate to consider three books which could contribute to a more rational management of a part of that environment. The first two contain information of a kind essential to those individuals empowered to undertake sound management of coastal areas and who thus may use the third as a manual of strategy. Each is composed of review papers and as such has a considerable potential value for the prospective audience. However, it is clearly not easy to ensure that the constituent papers have a uniform quality, and unfortunately these works do not escape this fate. Additionally, such works are evidently exposed to the danger of oversimplification and are peculiarly vulnerable to a critical quotation of counter examples; wisdom would therefore suggest that exaggerated claims regarding objectives and scope should be avoided. Because such books cover a wide field, much of it beyond the scope of expertise of the individual, the books' reviewer must judge the whole upon those sections in which he has some knowledge. Each of us must surely be well aware of the ease with which the vital reference is missed and of the appalling deficiencies of one's own knowledge; therefore carping criticism is an idle exercise.

Marine Ecology, volume 1, part 3, which is a part only of an ambitious, five volume, multi-part work, has the misfortune to suffer all the faults noted.

The publisher informs the prospective reader, drawn hopefully from a professional and lay audience, that it is intended "as an exhaustive systematic exposition summarizing and evaluating information obtained thus far on living systems in the sea and littoral areas". In six chapters, it deals with substratum, pressure, dissolved gases, organic substances, ionizing radiation and factor combination. Although one must be impressed both by the laudable and worthwhile objectives expressed and by the useful contribution which this work will make, one is left with an overwhelming sense of disappointment in its execution.

From internal evidence, one concludes that the information explosion has obliged the publisher to limit the number of references quoted, but why with respect to substratum, for example, are so few references quoted for the period since 1965? Why too are illuminating contributions ignored? As an example among several, is the work of D. P. Wilson who has contributed so much to the understanding of the mechanism of settlement by littoral invertebrates really not worthy of inclusion here?

The inconsistency between pages 1250 and 1257 regarding the ecological importance of the mineralogical composition of sediments is worrying, but should have been resolved during editing. Much more disturbing are the faults typified by that on page 1274 relating to the migration of littoral diatoms. Contrary to the statement contained therein, the ability to undertake tidal or diurnal migration is not confined to the naviculoid diatoms, nor are the *Hantzschia* spp. particularly outstanding in this respect. Indeed, a wide literature gives a very different view of this aspect of unicellular plant behaviour, which is exhibited by *Euglena* sp. and dinoflagellates in addition to the diatoms.

Regretfully, one must conclude that this is a useful, though not completely accurate, introductory work which fails to match the publisher's claims. This is a very great pity, for there is an undoubted need for an exhaustive work based on this conception and one hopes that in future parts such pitfalls will be

avoided and the ambitions of all concerned with them realized.

The Estuarine Environment consists of eight papers presented at the symposium held to mark the inauguration of the Estuarine and Brackish-water Sciences Association. The papers thus offered are concerned to present an up to date introduction to some aspects of the physics, chemistry and biology of estuaries; this they do with particular reference to those of Britain. The more outstanding papers are those of K. R. Dyer, R. L. Jefferies and P. R. Walne concerned with sedimentation, holophyte nutrition and the importance of estuaries to commercial fisheries respectively. With a multidisciplinary audience in mind one would have hoped, for the benefit of the non-botanist, that some clarification of the status of *Spartina,* other than the bald reference to it as *S. anglica,* would have been made.

The paper by H. Milne and G. M. Dunnet is concerned with the productivity relationships of the Ythan estuary, Aberdeenshire. They and co-workers have quantified the trophic ecology of some fish, *viz.,* goby and flounder, and birds, *viz.,* oystercatchers, greater black back and herring gulls and eider; although other trophic relationships have not been quantified, food webs for the mud-flat and mussel bed communities are presented. Apparently, *Carcinus* and *Littorina* resident in the Ythan differ, in their trophic ecology, from populations resident elsewhere; an elaboration of results with respect to these species would have been a most valuable addition here. Hopefully, this work will be published elsewhere shortly.

In general this is a book which does much of what it sets out to do; it is, however, an expensive purchase at £3.50; indeed, at this price the reader is surely entitled to a more uniform presentation of the figures than the uneven quality provided.

The eleven papers of *Coastal Zone Management* are concerned to provide a unified approach which embraces politics, conservation, social needs, problems concerned with shipping and ocean installations, and marine waste disposal systems. This is a valuable

work which demonstrates clearly both the conflicting interests and the intrinsic problems facing those who would see coastal areas managed rationally. It is unashamedly devoted to the problems of the USA. As such, knowledge from other sources is not used fully and thus its value to the cosmopolitan audience may be reduced. Truly outstanding is the exposition by E. A. Pearson of the issues which face the would-be manager of effluent releases. Too often, treatment and the pipeline have been regarded as mutually exclusive solutions to the waste disposal problem; that this is not so is adequately demonstrated in this clear account.   E. J. PERKINS

Matter and Life

Molecules to Man. By Sir George Porter, Richard J. Harrison, Paul R. Ehrlich, D. C. Phillips, G. V. J. Nossal and Chapman Pincher. Pp. 410. (Heinemann: London, December 1972.) £2.90.

SOME thirty years ago a series of talks introduced by Sir William Bragg were published by the BBC. Their intention was to show the continuity of principle between studies of atoms and molecules and the behaviour of genes, cells and organisms. The same idea seems to underlie the series of lectures at the University of Sydney which are collected in this book.

It certainly underlies the introduction by Bragg's successor, Sir George Porter, with his elegant account of theories of matter and of life. These connect very neatly with the nucleic acids and proteins which Professor Phillips uses to authenticate, as it were, the mechanism of heredity. Perhaps genetic principles are taken too much for granted at this point, for at the next step we find Professor Nossal grappling with immunity, a problem the crux of which is variation as much as heredity. Indeed, Burnet's theory of clonal selection among variant cells may be seen as assuming three levels of genetic control in variation. But it leads us to ask which of these levels are in the nucleus and which in the cytoplasm, which operate through DNA and which through RNA.

Nossal passes on to connect the immunity system and the study of cancer. He separates cancer induced by chemical carcinogens, cancer propagated by viruses (or proviruses), and cancer as an embryonic property. In immunity reactions these classes may differ but need they be mutually exclusive? Nucleus and cytoplasm as places of origin must be mutually exclusive. This separation is the inescapable one.

From immunity it is a long jump to the environment. Here Professor

Ehrlich is concise and effective. His arguments are by now well known. But behind the visible issues are conflicts of vested interest which need to be better known. They are of two kinds. One is between rich people or advanced countries who produce (and consume) too many goods and poor people or backward countries who produce too many children. The other conflict is between people who are accused of exploiting the physical sciences to the damage of the environment, and people who, mainly on biological evidence, make this accusation.

To recognize these conflicts is to take one step towards resolving them. A second is to recognize that beneath them are instincts for competition between people who firmly believe that they differ in intelligence. Such properties, whether of competitiveness or intelligence, have dominated man's past and, since they are inherited, they are not likely to be dismantled by exhortation. They therefore threaten us with uncontrollable dangers as the world's population approaches the limit which Ehrlich foresees.

To conclude, Mr Chapman Pincher gives his candid views on what the public should be told about science. He reveals the dilemma of the communicator who has to believe in the education of the masses (our masters, he says) although their demand for horoscopes makes him doubt the good it has done them. What they want is stories of sex reversal, instances of sex violence, and perhaps arguments for sex equality. Some of these Mr Pincher is able to provide.

At this point the reader may turn back to the middle of the book. Here there might have been some biological evidence which would have helped the discussion of sex in a serious way. Instead a hundred pages have been inserted on porpoises, pages unconnected with the rest of the book. It is as though the editor wished to persuade us that the appearance of design in his compilation was quite accidental. But perhaps indeed there was no editor.
                                          C. D. DARLINGTON

"Pop" Propellants

Ignition!—an Informal History of Liquid Rocket Propellants. By John D. Clark. Pp. xiv+214. (Rutgers University: New Brunswick, New Jersey, March 1972.) $10.

THE title of this book is a little misleading, for the dominant topic is propellant chemistry rather than the "ignition" problem, and in my view the suggestion that the contents are "informal" is an understatement. The style is often personal to the point of

embarrassment, though it certainly conveys the atmosphere behind the security curtain which usually screens this field of science from the general public.

The author, Dr Clark, was a senior propellant chemist with the United States Navy and Army for more than 20 years and is well qualified to explain the development of various rocket propellants from contemplation to completion or more frequently catastrophe! In many instances the workers are in an exasperating situation which, as usual, is funny to the onlooker (remember the case of George's shirt in *Three Men in a Boat*?), and while reading these sections I received many doubtful glances from fellow rail passengers. In order to follow large parts of the text, a knowledge of organic chemistry to at least "A" level is required, and the layman would have to be particularly interested in rockets to plough through all the material. The book should, however, be read by anyone with a degree interested in entering the aerospace, propellant or explosive fields, since it contains a lot of background information which is difficult to obtain elsewhere.

Students of the history of science will find the content strongly biased to the American achievements, and even these are regarded from the service rather than the university or industrial point of view.

The presentation is generally pleasing, with few typographical errors. However, I would have appreciated more photographs and diagrams.

In conclusion, the publication of this book gives an intriguing insight into the propellant community upon whom it undoubtedly exploded.
                                          J. SWITHENBANK

Mathematical Russian

Russian for the Mathematician. By S. H. Gould. Pp. xi+211. (Springer: Berlin and New York, 1972.) 27.60 DM; $8.80.

THIS book is the outcome of a project, sponsored by the American Mathematical Society, for a "crash course" in Russian, precisely adapted to the needs of mathematicians.

In the resulting course, compiled during a nine-months leave of absence from his duties as Editor of Translations for the American Mathematical Society, Dr Gould has approached a difficult task boldly, and with due attention, not only to the linguistic needs of his potential readership, but also to their intellectual aptitude. Basing his method on the assumption that "the vocabulary of the Russian language . . . makes a particular appeal to the

systematizing mind of the mathematician", he introduces vocabulary on the basis of groups of cognate words, explaining their derivations and connexions in an illuminating and memorable manner—if with occasional side-tracking into anecdotal material, or the considerations of historical and comparative phonology, which, although diverting and instructive, seem a little out of place in a brief course of this kind.

The lexical and grammatical material is presented in a clear and orderly manner, and, except for a few *exotica* in the early pronunciation exercises (the probability of *kot*—tomcat, *žuk*—beetle, *žoh*—swindler, *trup*—corpse or *yut*—quarterdeck, occurring in mathematical papers seems extremely small!) the grammar is illustrated by examples such as "the problem reduces itself to such a choice of the function for which the integral has the least value" or "we shall explain some questions of the theory of generalized functions constructed by S. L. Sobolev and L. Schwartz". There are, unfortunately, a few slips, perhaps the most serious being the statement that the genitive of negation is an optional, not an obligatory, construction.

Again catering to the specific needs of his readership, who will, presumably, have their attention drawn to Russian mathematical papers by a notice in *Mathematical Reviews*, Dr Gould recommends the system of transliteration favoured by that journal (although it differs somewhat from both the international and standard American versions). Less happy is his suggestion that the student should "invent" names for those letters of the Cyrillic alphabet which have no English equivalent. It would surely have been far more beneficial to have taught the Russian names for letters—one can visualize a situation of considerable confusion, if, say, in an enquiry by telephone to a library, a follower of Dr Gould's suggested system attempted to spell out a title, saying "zee-check" for "zhe", or "eshch" for "shcha".

In general, however, this book tackles a difficult task straightforwardly and competently. Its selection of texts for continuous reading advances from elementary analytical geometry and calculus, through number theory, rings and fields, to Baire classifications, mathematical logic, Hilbert space and topology. Little provision, however, is made for the applied mathematician, save for one elementary text on the addition of vectors and a short passage on partial differential equations. In view of the vast literature on applied mathematics currently being produced in the Soviet Union, this is, perhaps, the most serious deficiency of the book.

VERA RICH

Dyslexic Disabilities

Dyslexia and the Individual. (A Study of Reading Difficulty in "Word Blind" Children.) By Patrick Meredith. Pp. 190. (Elm Tree: London, November 1972.) £2.35.

IT would be easy to find fault with this book. There is no systematic marshalling of evidence, nor do any very firm conclusions emerge at the end. Clearly, however, Professor Meredith did not intend it to be that kind of book. What is being offered is not a systematic treatise on dyslexia but some personal reflexions.

Two main themes emerge. In the first place Professor Meredith delivers a blistering attack on traditional psychometrics (i.e., the alleged "measurement" of IQs, reading ages, and so on). He quotes with approval Eddington's dictum that "we can make nothing of measures without any note of the objects and circumstances to which they refer", and he points out that, when a child is being tested, the "circumstances to which (he) is responding . . . usually include a great deal more than the particular test-items on which the psychologist is concentrating". His second theme is that we should try to become more sensitive to what happens when people are exposed to different spatial and temporal sequences. "Laterality", he tells us, "is full of surprises".

The attack on psychometrics seems to me undoubtedly correct. I also agree that dyslexic children often fail "to co-ordinate, in time, their perceptions of space". There is still much in the book, however, which I find obscure, and there is even a certain amount which I suspect to be nonsense; for example, "The space-time of the child is a field of events, curled up and carved up in the convolutions of his cortex". On page 77 he promises a further book devoted to "ortho-chorics", which he refers to as a kind of "behavioural geometry". From the present book the case for such a science is by no means made out, but here one must suspend judgment until more details are published.

I have two further comments. First, it seems to me misleading that the book has been given the sub-title, "A Study of *Reading* Difficulty" (my italics). Professor Meredith would, I am sure, be the first to agree that for many children with the dyslexic cluster of disabilities reading is the least of their problems; and I think it should be stressed that, in spite of the incorrect associations with the Latin word *lego*, dyslexia is not just a difficulty with reading. Secondly, I am surprised that Professor Meredith shows so little enthusiasm for the work of Skinner. The "cumulative record", used by Skinner and his followers to provide a spatial representation of an organism's behaviour over time, is just the kind of notation which he might have been expected to favour, while Skinner's concept of the "discriminative stimulus" is one which forces experimenters to take serious note of the particular "circumstances" in which an organism's responses occur. Professor Meredith's views seem to me to have more in common with those of Skinner than perhaps he realizes.

T. R. MILES

Radiation Protection

An Introduction to Radiation Protection. By Alan Martin and Samuel A. Harbison. Pp. xi+216+4 plates. (Chapman and Hall: London, October 1972.) £1.95.

THIS book is intended to introduce those who have a science education to "O" level or equivalent standard to the principles and practice of radiological protection. Those persons most likely to find the book of value are trainee technicians and health physics monitors who will become responsible for the day-to-day control of radiation hazards in nuclear power stations, research establishments, hospitals and industrial premises where employees are exposed, or potentially exposed, to ionizing radiation.

The book contains seventeen chapters and at the end of each there is a summary and a number of revision questions which could be useful for both student and teacher at the level of City and Guilds examinations. The first few chapters deal with elementary theory of the structure of matter, radioactivity and radiation units. The middle chapters are on protection standards and methods of monitoring. The later chapters introduce practical aspects such as waste disposal, legislation, transport regulations and radiation emergencies, and these will be of particular interest as this material is not readily available in such an easily readable form.

Two chapters are of lower quality than the rest, one on "Biological Effects of Radiation" and the other on "The Internal Radiation Hazard". The authors could improve the former by the use of more up-to-date material from the excellent summary of the subject published as *Radiobiological Factors in Manned Space Flight*.[1] The latter is too short for such a complex topic. Its readability could be improved by a more liberal use of diagrams to illustrate metabolic pathways for ingestion and inhalation. This chapter also contains some errors of fact. In one

place, for example, bone is stated to be the critical organ for inhaled plutonium but this is not the case for insoluble compounds. At another point the wildly erroneous statement is made that "the rate of excretion of any substance from the body is approximately exponential". Here the desirable mathematical model seems to have been substituted for reality.

Apart from these small criticisms the book is entirely satisfactory and can be recommended to those teaching or learning elementary radiological protection theory and practice.

G. W. DOLPHIN

[1] Langham W. H. (ed.), *Radiobiological Factors in Manned Space Flight* (National Academy of Sciences, Washington DC, 1967).

Temporal Processes

What is Time? By G. J. Whitrow. Pp. 191. (Thames and Hudson: London, September 1972.) £2.

VIEWED simply as a popular exposition of a complex and difficult scientific theme, Professor Whitrow's latest book —an expanded version of four BBC Third Programme talks on the nature of time—is a remarkable *tour de force*. Its topics range from the Mayan conception of time to the ideas of Einstein and Minkowsky, from water clocks to atomic clocks, from the fossil record to human memory, from biological evolution to cosmic evolution, from ancient religious beliefs to modern philosophical doctrines. Professor Whitrow has managed to combine these and other facets of his vast subject into an integrated whole in which each facet illuminates and is illuminated by the others.

But this book is more than an extraordinarily successful popularization. It is also a perceptive historical account of the biological, social, religious and philosophical influences that have shaped Western ideas about time and temporal processes. Throughout most of human history time has been perceived as being essentially cyclic. In man, as in other organisms, diurnal, monthly and annual rhythms have become internalized through evolution. Moreover, except in highly industrialized societies, everyday life has always been dominated by the cycle of day and night, the ebb and flow of the tides, the progression of the seasons, the life cycles of plants and animals. The cyclic view of time was further reinforced by observations of planetary motions, which were thought—and are still thought by many—to govern · the subtler rhythms of men and nations. With the rise of Newtonian mechanics and of the technology that sprang from

it, Newton's view of a universal time, flowing "equably without relation to anything external", gradually displaced the ancient notion of cyclic time. Yet the Newtonian vision of the world differs almost as much from the modern one as from the one it displaced, for Newton believed that the world and its creatures had been shaped and set in motion by the hand of God only a few thousand years earlier. The modern view (still fragmentary and incomplete) —that the physical universe and the biosphere are the results of evolutionary processes—began to take shape only toward the end of the 18th century, and only during the last few decades have we been able to make reliable estimates of the time scales involved. Despite its brevity, Professor Whitrow's account of these developments, illustrated by aptly chosen quotations from literary, philosophical and scientific sources, is clear and well balanced.

On a third level, the book addresses itself to abstract philosophical doctrines. Professor Whitrow's skill in extracting the essence of a philosophical argument and presenting it in clear, simple language is reminiscent of Russell's. His critical technique relies heavily, and to excellent effect, on confronting doctrines in "pure" philosophy with relevant empirical evidence and theories from psychology, biology and the physical sciences. I especially enjoyed (though I was not always in full agreement with) the critique of Kant's views, the comparisons among absolute time, relational time and relativistic time, and the discussion of the transitional nature of time and the failure of current theories to come to grips with it. Professor Whitrow summarizes his own philosophical position in the book's final paragraph: "Although our perception of time has many subjective and even sociological features, it is based on an objective factor that provides an external control for the timing of our physiological processes. This objective factor is what we call physical time. It is an ultimate feature of the universe and its relationship with observers, particularly fundamental observers, which cannot be reduced to anything else. But this does not mean that it exists in its own right: it is an aspect of phenomena. The essence of time is its transitional nature. That this has given rise to so much argument down the centuries is not surprising, for, in the words of Whitehead, 'it is impossible to meditate on time and the mystery of the creative passage of nature without an overwhelming emotion at the limitations of human intelligence'."

Because of its scope, depth, readability and scholarly quality, this book, though intended for the general reader, is also admirably suited to serve as a text for an undergraduate seminar. Its

value in this capacity would be enhanced by the addition of some bibliographical notes and a list of references, which, it is to be hoped, will be added in subsequent editions.

DAVID LAYZER

Spectroscopy

Spectroscopy. Edited by D. A. Ramsay. Consultant editor, A. D. Buckingham. (MTP International Review of Science. Physical Chemistry, Series One, Volume 3.) Pp. 338. (Butterworth: London; University Park: Baltimore, Maryland, 1972.) £10; $24.50.

THIS volume is one of the first of a new series of comprehensive scientific review volumes produced by the Medical and Technical Publishing Company. Chemistry as a whole is covered in thirty-three volumes; this is volume 3 of the thirteen volumes devoted to physical chemistry. It consists of eight chapters of about forty pages each, these being independent reviews by distinguished contributors of various special fields of current interest.

The book is an undoubted success. All of the authors speak with authority on their subjects, and the subjects have been well chosen, although I am sorry that there is no chapter reviewing some of the more exciting experiments being done currently with lasers, double resonance spectroscopy, and suchlike. The reviews are indeed comprehensive, and in most cases report developments of the past ten years (rather than the last two years) in the field reviewed. Most of the readers will already be spectroscopists of one form or another. The volume has more in common with the series *Advances in Spectroscopy* edited by H. W. Thompson and published by Interscience, which ran to only two volumes (1959 and 1961), than it has with *Annual Reviews of Physical Chemistry* or *Annual Reports of the Chemical Society*. Its closest competitor today might be the appropriate volume of the Chemical Society *Specialist Periodical Reports*. The book is well produced, although it is quite expensive.

It is at present planned to republish the entire series every two years. If this plan is maintained, I think the style of the articles is likely to change from those in the present volume to something more akin to a catalogue of recent progress; I would regret this change, since such articles are less valuable and already exist in various rival publications. Either the subjects reviewed in the next volume should show little overlap with those reviewed here, or an interval of five or six years would be more appropriate if the style of the articles is to be maintained.

IAN M. MILLS

Non-molecular Solids

The Structures of Non-molecular Solids: a Coordinated Polyhedron Approach. By Graham M. Clark. Pp. xii+365. (Applied Science: London, 1972.) £9.

THIS book contains some short introductory chapters on sphere packing, crystal geometry, coordination polyhedra, and defect solids, and a short final chapter on lattice energies. Discussion of the relation of physical properties to structure is qualitative and on an elementary level. The principal part of the book is an account of the crystal structures of inorganic compounds (predominantly oxides and halides) arranged according to the way in which the coordination polyhedra (including planar triangular and square groups) share vertices, edges, and/or faces. Most of the structures are also described in terms of the closest packing of the larger ions. The book is necessarily concerned largely with structures based on tetrahedral and octahedral coordination and, in spite of the title, some molecular crystals are included. On the other hand, structures of very low coordination are not described in terms of the simple 2- and 3-dimensional nets which provide such elegant descriptions of a number of crystal structures. The omission of the simplest 3D 4-connected net leads to the description of the diamond structure as "that of sphalerite, except that carbon atoms occupy both the Zn and S sites". There are descriptions of a few structures of coordination number greater than 6, but the book does not cover the coordination numbers greater than 12 characteristic of many intermetallic compounds.

In general the descriptions are accurate and they are illustrated by many diagrams, some of which present novel views of the structures; a few should be redrawn. The grammarian might object to the statement· that "one of the most polymorphic substances known is silica"; objection should be taken to the descriptions of K_2SbCl_5 and K_2PdCl_4 as defect structures because this term is used in a different sense in chapter 4, and to the description of Fig. 1.15 (which should be rotated through 90°) as "The true (rhombohedral) unit cell of the ccp (fcc) arrangement". The opening sentence of the book: "High density and symmetrical external shape are two characteristic physical properties which distinguish crystalline solids from other states of matter" illustrates the dangers of generalizations.

Since this book is largely developed from other texts and secondary sources (though some references are given to the original literature) we must consider the merits of its characteristic feature,

namely, the systematic description of structures in terms of the way in which the coordination polyhedra are linked together. First, there are three types of model (or illustration) that can be made of many simple inorganic structures, the ball-and-spoke, close-packed sphere, and polyhedral (coordination group) model. Exclusion of the first of these leads to clumsy descriptions of certain simple structures, for example, that of diamond noted above, the NaCl structure as one in which octahedral coordination groups share all twelve edges, and the antifluorite structure as one in which tetrahedral groups share all six edges. Certainly structures such as those of ZnS, PtS, and NbO are more simply described in terms of 3D nets than as assemblies of coordination polyhedra. Second, the description of structures in terms of the coordination polyhedra around the metal atoms (ions) tends to minimize the importance of the environment of the anion, a shortcoming which is also a feature of many descriptions of structures in the original literature. Third, the strictly systematic geometrical approach to structures has additional value if we wish to compare the geometrically possible structures with those actually found, and to discuss why certain structures are not adopted. Conversely, the (geometrical) impossibility of building structures for compounds A_mX_n from certain coordination polyhedra would seem to be the reason for some of the "anomalies" which puzzle the author in applying the radius–ratio concept to simple ionic crystals, to the structures of which it has, in fact, only a very limited relevance. Finally, most readers, whether students or teachers, find difficulty in visualizing many structures from plane illustrations, however well they may be drawn, and I am rather doubtful about the value of the polyhedral representations of many of the more complex structures.

Although I look upon the material of this book as an integral part of structural inorganic chemistry, this viewpoint is not yet universally adopted, and it is unlikely that the book will be acceptable at the present time as an undergraduate text. It is my opinion that a real understanding of the geometry of crystal structures can be gained only from the study of models, preferably built by the student. This book could provide useful supplementary reading in places where the teaching of inorganic chemistry has advanced to the stage of including model building as part of the practical curriculum. Unfortunately, even after sixty years of X-ray diffraction many teachers of chemistry do not appreciate, or are unwilling to acknowledge, that the structures and

properties of solids form a large and important part of inorganic chemistry, though the inclusion in the syllabus of structural organic chemistry of comparable complexity is not questioned. An early introduction to repeating patterns and some solid geometry would help to produce a generation of teachers willing to venture beyond the familiar finite groups of atoms.

A. F. WELLS

Lunar Data

The Moon. Edited by S. K. Runcorn and H. C. Urey. (International Astronomical Union Symposium held at the University of Newcastle upon Tyne, March 1971.) Pp. xvi+471. (D. Reidel: Dordrecht, Holland, 1972.) Dfl. 110.

THIS is the report of the second IAU symposium to be devoted to the Moon. While it was not restricted to results gained by space technology, comparison with the first symposium held ten years earlier does show how the subject has developed out of all recognition in consequence of the various Luna and Apollo missions. The growth is alarming, but the editors do call attention to the agreeable feature that it offers to graduate students in the physical sciences a great opportunity to share in interpreting this vast corpus of information. Students who seize this opportunity can have the assurance that they are working on problems of rewarding significance.

The book comprises well prepared and presented texts of most of the papers read at the meeting. There are forty of these, classified into nine sections dealing, in brief terms, with lunar mechanics, lunar surface, Apollo missions, petrology, tectonics, physics of lunar samples, interior, orbit, origin and evolution. A majority of the papers report very recent observational and experimental work and its fairly immediate interpretation. Only a few deal with more general theoretical problems, chief amongst these being the papers by Urey and Levin who discuss the origin and evolution of the Moon, or at any rate survey the significance of new discoveries for these topics. Urey remarks, "No one has changed his mind in regard to the origin of the Moon, and we can only conclude that all the evidence from the space programme is indecisive in regard to this question". This sums up the impression one forms for oneself on reading this admirable compendium of so much of that evidence. However, the fact that such a great deal has been assembled in one volume of manageable size should itself help those who are concerned with the larger problems to discern the more general significance of the evidence, and so maybe to make better use of it.

In this connexion one might suggest that any future compilation of this sort might well include a glossary designed to help the more general reader to understand the language of the specialists in each section.

The attractiveness of the book is much enhanced by the frontispiece—a charming snapshot of the founding fathers of the modern study of the Moon, A. A. Mikhailov and H. C. Urey.

W. H. McCREA

Regenerative Capacity

Organ Regeneration in Animals: Recovery of Organ Regeneration Ability in Animals. By L. V. Polezhaev. Pp. ix+190. (Charles C. Thomas: Springfield, Illinois, 1972.)

POLEZHAEV is best known for his early work in which he persuaded frog limbs to regenerate after amputation. Normally tadpoles can, and adults cannot, perform this feat. To restore the capacity lost in ontogeny he, Rose, and Singer independently used different methods, but each with some success. It is natural to turn from such work to other systems in which regenerative capacity is absent or limited, to apply the lessons learned. Two such systems loom large in this book—the irradiated urodele limb, and mammalian tissues. It is claimed that the former can recover regenerative capacity after the administration of several substances—rat muscle homogenates, rat liver RNA, or milk protein.

The author reviews recent work, much of it from the USSR, on mammalian tissues, for the benefit of clinicians who are, of course, directly concerned. Unfortunately, his treatment is neither entirely summary nor sufficiently detailed to allow the reader to judge the experimental evidence to which he refers. The section on the central nervous system with which the work ends is particularly difficult to assess, since the claims to have induced DNA synthesis, nuclear division, and cell division (as well as endopolyploidy) in mammalian cerebral neurones by treatment with tissue extracts are uncritically presented.

Above all, however, the editing of the English version of this book is so awful that its message can only be approached through a haze of words misspelled, misused, or simply invented. The syntax also is odd. In the interests of rapid, or of cheap, publication of translated texts one should, in my opinion, be tolerant in such matters, but this book goes too far. The reader's irritation transfers to the substance of Polezhaev's arguments, some of which certainly need what help they can get from a faultless exposition.

D. R. NEWTH

Magnetic Resonance

Magnetic Resonance. Edited by C. A. McDowell (MTP International Review of Science. Physical Chemistry, Series One. Volume 4.) Consultant editor, A. D. Buckingham. Pp. 365. (Butterworth: London; University Park: Baltimore, Maryland, 1972.) £10; $24.50.

HERMES TRISMEGISTUS, who knew everything and, it is said, wrote it all down in 36,525 volumes, is to be emulated a few thousand years later by the MTP International Review of Science, of which the present book is volume 4 of the first series for the treatment of physical chemistry. Meanwhile, the theory and practice of magnetic resonance have developed notably, and the editor (who now, alas, is needed) has attempted to provide a glimpse of the advances in the subject between 1967 and mid-1971. The ten chapters cover nuclear spin relaxation in gases (Bloom), n.m.r. studies of molecular motion in solids (Allen), Mössbauer spectra (Sams), n.q.r. (Chihara and Nakamura), ^{13}C relaxation (Lyerla and Grant), liquid crystal spectra (Bulthuis, Hilbers, and MacLean), electron resonance in gases (Brown), optical detection (Kwiram), irradiated organic crystals (Iwasaki), and the biological applications of e.s.r. (Bolton and Warden).

Many of the topics treated correctly reflect the modern tendency in magnetic resonance towards either the study of physical phenomena or biological systems; the volume teeters on the brink of ecodoom in only one place (page 351). Nevertheless, there are topics omitted whose inclusion would have made a truer representation of the present activities: Fourier transform techniques in n.m.r., n.m.r. of biological systems, and chemically induced spin polarizations are not included. The authors have written in a variable fashion; most chapters have introductory material, but vary in the rapidity with which they become synoptic reviews. It is important for the editors to establish whether the contents are to be comprehensive and detailed, or essays on topical subjects; since the *Specialist Periodical Reports* of the Chemical Society attempt the former, and more cheaply, I would prefer the second alternative. There is no reason why both cannot be combined: a review of the principles and status of the subject could be followed, but clearly distinguished from, a thorough and comprehensive specialized review of its progress. In any case, the non-specialist reader would be helped if in future volumes each chapter contained a synopsis of the most notable advances that had been made, and a brief résumé of the present centres of interest.

The volume has neither author nor subject index, although we are promised one for the whole set. This omission is inexcusable and suggests quite clearly that the books are aimed at libraries whose hitherto generous bosoms can embrace complete sets. Private bosoms, who might muster £10, will, and should, feel cheated.

P. W. ATKINS

Logic of Mathematics

What is Mathematical Logic? By J. N. Crossley, C. J. Ash, C. J. Brickhill, J. C. Stillwell and N. H. Williams. Pp. ix+82. (Oxford University: London and New York, November 1972). £1.40 cloth; 70p paper.

THIS little book grew out of a short course of lectures to non-specialists at Monash and Melbourne, and it retains much of the freshness of that venture. The tone is set by the authors' opening declaration: "Mathematical logic is a living and lively subject. We hope that this will be conveyed by the somewhat unconventional style in which this book is written." On the whole, books on mathematical logic tend to be either systematic textbooks, which their readers are meant to work through slowly and methodically, or else more or less perfunctory popularizations of the subject; but the present authors have attempted something rather different, which should be of substantial benefit both to logical studies and to education as a whole. In a brisk review of mathematical logic, covering all its main branches, they give a succinct account of the central problems and results, in which, despite the informality of their style, they treat seriously the ideas and methods that really matter. Non-logicians to whom abstract thought is not entirely foreign should thus be able to gain some knowledge of what kind of subject mathematical logic is, and of where it is located on the academic map; while readers who subsequently embark on serious study of this subject will do so with an initial orientation to assist them in finding their bearings. For those who are inspired to read on further for themselves, a helpful reading list is provided.

The book comprises an introductory historical survey (from about 1850 to 1963), followed by separate accounts of the completeness of the predicate calculus, model theory, Turing machines and recursive functions, Gödel's incompleteness theorems, and set theory. As might be expected, the chapters are not all equally successful; but the best of them—particularly the ones on Turing machines and Gödel's theorems —are very readable and informative.

G. T. KNEEBONE

CORRESPONDENCE

Bad BBC Science

SIR,—Since I advised on the Horizon programme "Science is Dead—Long Live Science" variously described in your leader (*Nature*, **241**, 490 ; 1973) as "disastrous", "witless", and "dangerously infected with heresy", I would be grateful for the opportunity to make a few comments.

First, I must remark on the distressingly high proportion of gross errors of perception on which your writer based his judgments. The Vietnam films were very far indeed from "the most gruesome of the gruesome" ; the "defoliant" scientist was interviewed but not the "napalm" scientist ; nowhere was there a claim that science made the Vietnam war possible ; the scientist-turned-printer was not "offended" by the FBI, but described quite clearly how he was hounded out of his job ; the interview in West Virginia had as its whole point the complete corruption of the local government by the strip-miners and the effective disenfranchisement of the public ; Jonathan Beckwith neither gave alarming tales of genetic engineering nor said when civilization would end ; the New Alchemist made no claim to secret knowledge ; and it was a quite different group who have gone over to Sun worship.

Perhaps there were some deeper failings in presentation that enabled your reviewer to become so confused. If so, I and the producers would be very grateful for help. It seemed abundantly clear to us that each of the very different sorts of scientists presented in the programme were a small minority—the general indifference at the AAAS meeting was, we thought, a sufficient reminder of this. We thought also that the difficulties and contradictions in each reaction, systematically and sympathetically described by Beckwith, were made clear in nearly every case.

If I were to help in modifying the programme for a re-issue, I would start by putting more emphasis on one particular still shot. This is of a proud advertisement by North American Rockwell. It describes their development work on the B-1 bomber, the planned successor to the B-52 of saturation-bombing fame. Their triumphant slogan is "North American Rockwell—where Science Gets Down to Business". This phrase, so cleverly combining a straight description with an American idiom, has rich overtones in the political and moral dimensions. I strongly suggest that your reviewer reflect on that slogan ; from

that could come an appreciation of what the programme was all about.

Finally, I hope that your reviewer will, on reconsideration, regret that personal sneer at the physicist persecuted by the FBI, and also the most unfortunate arguments on the responsibilities of civil servants by which the reviewer justified himself. This lent neither strength nor dignity to his criticisms of the programme, and a retraction and apology would seem appropriate.

Yours faithfully,

J. R. RAVETZ

Department of Philosophy,
University of Leeds

SIR,—It is unfortunate that your attack (*Nature*, **241**, 490 ; 1973) on the BBC for irrationality in science programmes was itself so irrational. It used a device much favoured in debating societies, but surely to be abjured by a scientist with any pretensions to objectivity, namely falsely accusing the opposition of having made a certain statement and then proceeding to demolish it.

In stating that the Horizon programme "Science is Dead—Long Live Science" implied an absurdity, namely that the profession of science, not the political climate, made the Vietnam war possible, you underestimate the average viewer's intelligence and good sense and negate your own. "Implication" is in the brain of the beholder, and I for one caught no shadow of such an implication. The programme was making a quite different point, clear enough to an unbiased viewer, that the scientific weapons being used were based on investigations made for peaceful ends, not specifically developed by government scientists aware of their mission. Almost all your allegations are similarly off beam. To take just one more example, it is simply not true that the programme used Beckwith "as an excuse for alarming its audience with tales of genetic engineering". The programme was, in fact, making exactly the opposite point, namely that when Beckwith tried to interest the community in a (note) rational consideration of the possible consequences of chemical synthesis of a gene, he was so distressed by the alarmist furore that his action set off in the popular press that he desisted.

What impels me to write, rather than ignore such ill-founded criticism, is that your editorial castigated a courageous and original attempt to explore a real and important facet of the scientific world, namely the constant and insidious

worry about the hideous uses to which the most innocent scientific discovery may eventually be put. What gives Horizon programmes their continuing vitality is precisely these qualities of courage and originality. It is easy to make programmes which are aimed at blinding the public with science and how marvellous it all is ; it is easy too (as your editorials frequently demonstrate) to rail at the Establishment, and even easier to ridicule the thoughtful and rebellious young. It is not so easy to describe, quietly and objectively, an uncomfortable phenomenon in our midst—scientific heretics—and to discuss without hysteria a profound problem that troubles us all ; whether to continue to wrest secrets from nature that may be perverted to evil ends. In my opinion, this Horizon programme did just that, and did it extraordinarily well.

Yours faithfully,

F. PETER WOODFORD

Creation *vs* Evolution

SIR,—The decision of the State Board of Education in California to preach the doctrine of creation rather than to teach the theory of evolution in the state high schools has not only created a stir among the intellectuals of the world, but thrown a challenge to the entire scientific world to dispel myths about certain phenomena of the universe which are considered as status symbols of transcendental edicts of present day society. The letters of G. Vanderkooi, E. C. Lucas, and A. R. Smith (*Nature*, **240**, 365–366; 1972) and A. J. J. Hayward (*ibid.*, 492) support the existence of supernatural power which controls the universe. It is unfortunate that a plant taxonomist, A. R. Smith, could not visualize the process of evolution, which he ridiculed as a "tissue of lies". I, as a botanist, do not agree with him.

The concept of evolution is based on scientific facts, and reveals the truth of nature, although problems such as the origin of life and man's origin are still open for further studies. It is necessary to realize that evolution does not always mean the tracing out of the ancestry of organisms, but as a natural process that has been operating in the universe. Within the living organisms it is an essential natural process taking place as a result of interaction between the genomes and the ever changing environment. Genetic recombination, mutation and selection are the main wheels on which the vehicle of evolution is

proceeding to its never ending destination. Vanderkooi, who argued that there is no evidence to account for the process of macroevolution, is probably unaware of the fact that adaptive radiation is responsible for the evolution of higher taxa. True, there are certain forces in nature which cannot be readily explained in terms of science. This inability of science has often been taken up as a proof of the existence of a creator. It is increasingly evident that selection pressures direct the process of evolution. Although it is very difficult to interpret what is exactly a selection pressure, it is not ruled out that a scientist may come out with a model which unearths the hidden secret of selection pressures.

Vanderkooi pointed out that bacterial cells are as complex as any other living cells of the organism, and as such they cannot be considered as the primitive living organisms from which other organisms have been evolved. It is possible that all living organisms might have evolved from some primitive form (monophyletically), and further diversification within the evolved groups might have resulted in the evolution of different groups polyphyletically. The closer resemblance of the amino-acid sequence in cytochrome-C of wheat to that of animals rather than to cytochrome-C of fungi favours the polyphyletic origin.

On the other hand, the concept of creation is nominalistic, and has no place in scientific thinking. The doctrine of creation is a man-made catastrophe, and if it is continued to be advocated by man as a basic conceptual controversy, it is just like putting the clock back and will hamper the advancement of humanity.

To denounce the teaching of the theory of evolution, which has been nurtured by the cumulative efforts of hundreds of scientists for about 100 years, is to deny the legitimate rights of society to learn and understand the reality of the nature and the role of man as part of the natural and social world. If it is done it will become one of the greatest tragedies and educational failures of our time.

Yours faithfully,
C. R. BABU

Department of Botany,
University of Delhi,
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Use of IS, TWA and ILWS

SIR,—The present author (PA) is writing to request the increased use in *Nature* of initial-letter-word-substitution (ILWS). Unpublished studies of the PA show that the superficial-scientific-appearance-rating (SSAR) of a paper is most effectively increased by impersonal style (IS), technical-word-amplification (TWA) and ILWS. There is, moreover, a highly significant positive correlation between the SSAR of a paper and its peer-esteem-rating (PER). The PA hopes that *Nature* will cooperate in raising the PER of its contributors by encouragement of ILWS, as well as acceptance of IS and TWA.

Yours faithfully,
J. M. BARRY

Department of Agricultural Science,
University of Oxford,
Parks Road, Oxford OX1 3PF

Between Bees

SIR,—
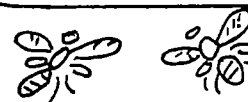
He's saying, "Go to Hive 2 tomorrow. They're *killing* bees at Hives 1 and 3".[1]

Yours faithfully,
F. J. MALONEY

Livermore,
California

[1] *Nature,* **241,** 171 (1973).

Obituary

Dr Stephen R. Pelc

STEPHEN R. PELC, who died suddenly on February 6, at the age of 65, was internationally famous for his pioneer work on the techniques of autoradiography and for his use of these techniques in cellular biological research. He graduated from the University of Vienna and published his first work from the Institut für Radiumforschung in 1931. In 1938 he came to Britain and, after serving in the forces during the war, he restarted his scientific work at the Hammersmith Hospital, London, first as a hospital physicist and then as a member of the MRC Radiotherapeutic Research Unit.

There he began his studies on the action of ionizing radiations on photographic film which led to his development of stripping-film autoradiography for obtaining high resolution autoradiographs of sections of biological material, work done with the enthusiastic collaboration of Dr (now Professor) I. Doniach and under the scientific directorship of the late Dr L. H. Gray.

Dr Pelc had the idea of using pliable photographic film stripped from Ilford stripping plates which were, at that time, being used in industry for other purposes. Kodak then produced the AR10 and AR50 stripping film to his requirements, giving far greater resolution, so that these have now become the standard materials for this form of autoradiography. Initially, when ^{131}I was the most readily available isotope, this technique was used by Professor Doniach and himself for studies on the thyroid gland under various physiological conditions. As other radioactive isotopes became available, however, the applications of autoradiography expanded rapidly so that it is now used throughout the world on many varied biological and medical research problems.

He is most famous for work begun in the early nineteen-fifties with Dr Alma Howard. By incorporating ^{32}P into dividing cells and removing all but the DNA by acid hydrolysis he was able to time the incorporation of ^{32}P into nuclear DNA. He showed that DNA synthesis did not occur after prophase, as had been believed previously from staining evidence, nor did it occur continuously throughout interphase. He and Howard showed that, for each type of nucleus, there was a particular period of interphase, which he called the "S" (synthesis) stage, during which the DNA content doubled; this DNA was stable and became divided equally into the two daughter nuclei. Before and after the "S" there was a gap in his knowledge of what metabolic processes occurred in the nuclei and, understandably, he named these "G_1" and "G_2". The period of interphase therefore could be extended if G_1 or G_2 became prolonged. These results were confirmed and extended considerably with the introduction of other isotopically labelled DNA and RNA precursors, particularly those labelled with ^{3}H.

Thus he laid the basis for the study of cell kinetics based on the timed uptake of isotopically-labelled precursors and their distribution into the cells derived from the initial, labelled mitotic cell. Of particular importance were his studies on the small intestine, in which

there is a constant replacement of cells, and on the skin where the processes of keratinization affect the DNA of the daughter cells.

Dr Pelc collaborated with many major research workers in autoradiographic metabolic studies on their own research problems. Thus his own interests extended from DNA over much of metabolic cellular biochemistry. By 1957, however, when he moved to the MRC Biophysics Research Unit at King's College, his main concern had again become DNA. He then showed, in a series of elegant studies, that the DNA of a wide variety of cells was not as completely stable as had been thought originally during the first flush of the DNA-gene concept. His work showed that sometimes as much as 50 per cent of the nuclear DNA was being turned over, the proportion of this "metabolic DNA" in any given nucleus apparently varying with the general metabolic activity of the cell.

For the past two years he was a member of the MRC external staff, working in the Division of Cellular Biology of the Kennedy Institute of Rheumatology in London. Here he extended his work on metabolic DNA, and showed that the metabolic DNA of splenic lymphocytes was considerably stimulated as a result of the immune response. He had also shown that metabolic DNA was of considerable significance in the process of ageing, and was currently very interested in the work of his collaborators, Dr M. Stroun and Dr P. Anker (Geneva) which showed that DNA can be passed from cell to cell. Thus it seemed likely to him that the metabolic DNA, which he saw as the expendable copies of the genic DNA, could act as a messenger between cells and so carry active gene messages to cells in which these genes were otherwise repressed.

Stephen Pelc was an outstanding scientist. A physicist by training, he was a cell biologist first and foremost, who used physics and mathematics adroitly in his biological research. Everyone who knew him was impressed by his gentle, genial kindliness, his readiness to help others and his good humoured philosophical approach to science and to life generally. He was an original thinker who designed his experiments decisively. Thus he was a pioneer, and pioneers rarely get the immediate recognition of their innovations. Sufficient time had elapsed from his development of autoradiography and his work on the timing of the nuclear synthesis of DNA for him to have been recognized as the authority on the techniques and on cell kinetics. The full significance of his discovery of the metabolic turnover of a fraction of nuclear DNA may yet take several years.

Second to science, his major interest was music, in which he found relaxation and mental refreshment. He was an accomplished violinist and leader of a string quartet which met regularly. He will be greatly missed by his fellow scientists who relied so heavily on him for his general scientific wisdom as well as for his specialized knowledge.

Announcements

Miscellaneous

The following have been elected **Fellows of the Royal Society**: **Professor Percival Allen** (University of Reading); **Dr Brigitte Alice Askonas**, (Immunology Division, National Institute for Medical Research, London); **Mr Francis Thomas Bacon** (Fuel Cells Limited of Cambridge); **Dr Alan Baker** (University of Cambridge); **Professor Neil Bartlett** (University of California at Berkeley); **Professor William John Granville Beynon** (University College of Wales, Aberystwyth); **Mr John Gatenby Bolton** (Australian National Radio Astronomy Observatory at Parkes, New South Wales); **Professor David Roxbee Cox** (Imperial College of Science and Technology, University of London); **Professor Leslie Crombie** (University of Nottingham); **Professor Harry Elliot** (Imperial College of Science and Technology, University of London); **Professor Douglas Scott Falconer** (University of Edinburgh); **Professor Geoffrey Alan Gilbert** (University of Birmingham); **Professor Harish-Chandra** (Institute for Advanced Study, Princeton, New Jersey); **Professor Richard John Harrison** (University of Cambridge); **Professor Harold Horace Hopkins** (University of Reading); **Dr Anthony Kelly** (National Physical Laboratory, Teddington, Middlesex); **Dr Egon Hynek Kodicek** (MRC Dunn Nutritional Laboratory, Cambridge); **Professor Jack Lewis** (University of Cambridge); **Dr Mary Frances Lyon** (MRC Radiobiology Unit at Harwell); **Dr Peter Bryan Conrad Matthews** (University of Oxford); **Professor George Francis Mitchell** (Trinity College, University of Dublin); **Dr Helio Gelli Pereira** (Division of Virology at the National Institute for Medical Research, London); **Professor Paul Emanuel Polani** (Paediatric Research, University of London); **Professor John Graham Ramsay** (Imperial College of Science and Technology, University of London); **Mr Lionel Edward Aston Rowson** (ARC Unit of Reproductive Physiology and Biochemistry, Cambridge); **Dr Monkombu Sambasivan Swaminathan** (Indian Council of Agricultural Research, New Delhi); **Dr Jamshed Rustom Tata** (Developmental Biochemistry, National Institute for Medical Research London); **Dr David Warren Turner** (University of Oxford); **Professor William Frank Vinen** (University of Birmingham); **Professor Paul Egerten Weatherley** (University of Aberdeen); **Professor Ronald Whittam** (University of Leicester); **Professor Alec David Young** (Queen Mary College, University of London.

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Population Pressure Diluted

THE British government's population panel, under the chairmanship of Professor C. R. Ross of the Central Policy Review Staff, has produced an exhaustive report of the possible effects of different levels of population in Britain in the next hundred years (*Report of the Population Panel*, HMSO, Cmnd. 5258, £0.90). It is at once clear that the panel's recommendations are well founded and that its approach to assessing whether or not Britain should have a population policy can be commended. In particular, the presentation to government departments of three alternative models of the British population for fifteen and forty years ahead when asking these departments for their views on the relevance of population trends was a wise move, the success of which will benefit other inquirers of these departments.

But what of the recommendations? The panel suggests that the government should not in future regard the level and rate of increase of the population with indifference but also, quite properly, it does not see the need for fiscal policy to influence the size of families in the foreseeable future. But the panel is loud in its warning that the government should not have a population policy that sets a definite limit for the British population at some time in the future. It is proper that the panel has steered clear of defining an optimum population, for there are no accurate ways of calculating this figure in terms of economic benefits to the country, but suggestions which have been made that the optimum British population should be 30 million, based presumably on the fact that only enough food is produced within Britain to feed this number, are quite sensibly dismissed by the panel on the grounds that "to frame policy in terms of 'targets' which take no account of the built-in momentum of the demographic process or the uncertainties about the extent to which population growth can be influenced by policy is neither sensible nor realistic".

It now seems that the population of Britain will increase from its present value of about 55 million to 64 million sometime during the first decade of the next century. It is brave of the panel, in view of the concern that has been expressed about the size of the British population, to come out and say that given a not too unstable world situation, Britain should be able to find means of accommodating any likely increase in population over the next forty years. There will also be little disagreement with the panel's view that Britain would be better off with a stationary population than with an expanding one, although such a situation is unlikely to occur in the near future. For those that take apparent delight in predicting that catastrophe of one sort or another is around the corner, the report brings little comfort. Professor Ross is quite clear in his recommendation that provided the rate of increase of population does not change suddenly the prospects for the next thirty or forty years are such that no drastic action is required.

Much of the uncertainty and confusion which has arisen in the past about the implications of population growth has been caused by a palpable shortage of information. Why do fertility rates change with no apparent rhyme or reason, the increase in Britain in the early 1960s in particular? Similarly, what are the factors which affect mortality, especially in children? To what extent do emigration and immigration affect population estimates? And with Britain now firmly entrenched within the European Economic Community the question has to be asked whether British people are going to move to Europe in increasing numbers or whether the Europeans will find the grass greener in Britain than in their homelands? The Population Panel has been equal to the challenge and the recommendation that a centre be set up for population studies is to be welcomed as indeed is the suggestion that it should be built at a university and that it should be closely connected to the economics, social sciences, biology and medical departments of that university.

Population, according to the panel, should become the responsibility of a senior non-departmental minister and a small group on population matters should be set up within the Cabinet Office together with an interdepartmental committee to coordinate all work on population. It is also recommended that the Office of Population Censuses and Surveys should also be expanded and strengthened, chiefly in order to analyse demographic data but also to commission research on population matters. A Minister for Population, as is admitted in the report, could not be effective without having at his fingertips a great deal more information on population than is now available. This, combined with the panel's assurance that the expected increase in the British population in the next thirty or forty years is not likely to cause difficulties, makes the need for a minister less immediate than the need for more research in demography.

Tunnelling for Trouble

THE British and French governments, having apparently learned nothing from their ill-starred Concorde project, seem bent on spanning the English Channel with a tunnel first proposed in the 1850s and which is unlikely now to be an economic proposition. In a memorandum on the subject published last week (*The Channel Tunnel Project*, Cmnd 5256, HMSO, £0.365), the Minister for Transport Industries, Mr John Peyton, says, to be sure, that "the project will only be undertaken if it is shown by the current technical, economic and financial studies to be a sound business proposition" but he has also spelled out a timetable for making a decision which is exceedingly tight. The document says that a treaty between France and the United Kingdom will be needed by July 31 this year and that preliminary works on the tunnel would begin this autumn with the prospect of a final agreement on the financing of the tunnel itself being signed early in 1975, just two years from now. There is no objection to the way in which the project has several intermediate decision points, but it is seriously to be questioned

whether an objective view of the economics of the tunnel could be formed in the next three months. Certainly it is hard to see why there should be such a rush to begin work on a project which is likely to cost far in excess of the figure of £366 million now quoted for the tunnel, and which is itself innocent of the not inconsiderable interest charges that would accrue in the next decade.

The objections to the tunnel project mount as the months go by. It is true, of course, that traffic between Britain and the mainland is increasing rapidly. The government document calculates that traffic of most kinds is now doubling every decade. The big uncertainty in the plan for a Channel tunnel is the extent to which enough of this increase could be attracted to the tunnel. No doubt the government is right to calculate that a through train service between London and Paris could put the airlines now operating on that route at a disadvantage, and it is also true that increasing congestion at Channel ports in the summer may persuade holiday makers that it would be better to put their cars on a train and make the journey across the water in relative comfort. But this business is unlikely by itself to make the Channel tunnel profitable. What really matters is what the future pattern of freight traffic will be, and whether the comparatively high yielding passenger traffic between Britain and the mainland, as distinct from the traffic between Dover and Calais, can be persuaded into the tunnel. The prices now being offered by Channel ferry operators are already competitive with those likely to have to be charged to make the tunnel profitable, there are difficulties in using continental freight cars and passenger carriages on British railways and the government's calculation of the cost of the tunnel leaves out of account the need to build new access roads to the coast of Kent so as to service the tunnel terminals. The biggest danger in the government's commitment to the Channel tunnel is that it may find itself, several years from now, controlling the competition across the Channel so as to create an artificial demand for the service it now proposes to provide.

What can be done by other means to accommodate the growing demand for cross-Channel travel? This is what the two governments should urgently be asking themselves in the weeks ahead. So far as passengers are concerned, there is plenty of scope for making the present system more efficient by improving the facilities for air travel which at present exist. Why is there, for example, no air shuttle service between London and Paris? Why are air fares so high and seats on aircraft so hard to buy? Where other kinds of travel are concerned, the government should recognize that there is a need for travel between Britain and the Low Countries, with Germany beyond, which is unlikely to be satisfied easily by a narrow link between Kent and the Pas de Calais. At least one sensible alternative to the Channel tunnel which should now be considered is the establishment of one or two substantial new ports on the east coast of Britain. The growth of East Anglian ports in the past few years shows where this demand applies. It might now be sensible to think of further developments along these lines, either on the Thames estuary or even on that never-never bit of Britain—the Goodwin Sands—which might provide sea links in their way as efficient as the tunnel now proposed.

In the long run, however, the government should pay more attention than it has to the possibility of forging a surface link between Britain and the continent. One possibility, lightheartedly dismissed in the document now published, is that there should be a bridge. Another is that deliberate attempts should be made to shorten the sea-link between Britain and the continent by means of barrages, land reclamation projects and the like. Although the government has often mentioned possibilities like these, it has never given them the serious consideration they deserve. The danger now is that it will be hustled into a rapid decision on the Channel tunnel without taking account of the effects that such a link will have on the whole pattern of transport between Britain and the rest of Europe.

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100 Years Ago
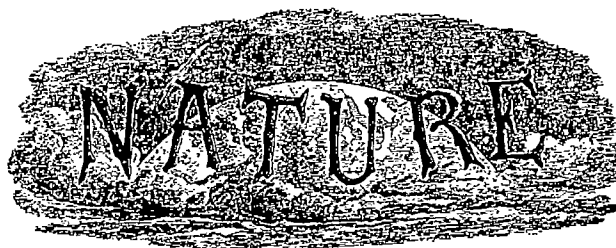
With regard to the question of the means by which animals find their way home from a long distance, a striking account, in relation to man, will be found in the English translation of the Expedition to North Siberia, by Von Wrangell. He there describes the wonderful manner in which the natives kept a true course towards a particular spot, whilst passing for a long distance through hummocky ice, with incessant changes of direction, and with no guide in the heavens or on the frozen sea. He states (but I quote only from memory of many years standing) that he, an experienced surveyor, and using a compass, failed to do that which these savages easily effected. Yet no one will suppose that they possessed any special sense which is quite absent in us. We must bear in mind that neither a compass, nor the north star, nor any other such sign, suffices to guide a man to a particular spot through an intricate country, or through hummocky ice, when many deviations from a straight course are inevitable, unless the deviations are allowed for, or a sort of "dead reckoning" is kept. All men are able to do this in a greater or less degree, and the natives of Siberia apparently to a wonderful extent, though probably in an unconscious manner. This is effected chiefly, no doubt, by eyesight, but partly, perhaps, by the sense of muscular movement, in the same manner as a man with his eyes blinded can proceed (and some men much better than others) for a short distance in a nearly straight line, or turn at right angles, or back again. The manner in which the sense of direction is sometimes suddenly disarranged in very old and feeble persons, and the feeling of strong distress which, as I know, has been experienced by persons when they have suddenly found out that they have been proceeding in a wholly unexpected and wrong direction, leads to the suspicion that some part of the brain is specialised for the function of direction. Whether animals may not possess the faculty of keeping a dead reckoning of their course in a much more perfect degree than can man ; or whether this faculty may not come into play on the commencement of a journey when an animal is shut up in a basket, I will not attempt to discuss, as I have not sufficient data.

CHARLES DARWIN

From Nature, **7**, 418, *April* 3, 1873

OLD WORLD

Nuclear Power: Weinstock at the Helm

BRITAIN'S nuclear design and construction industry has finally been restructured with Sir Arnold Weinstock ultimately in charge.

Under the government's proposals, a new company is to be formed, 50 per cent of which will be owned by Sir Arnold Weinstock's General Electric Company, 35 per cent by a shareholding company into which other members of Britain's existing nuclear power industry can buy, and 15 per cent by the government held through the United Kingdom Atomic Energy Authority.

It is clear where the power is to lie. Mr. Peter Walker, Secretary of State for Trade and Industry, announcing the government's decision in the House of Commons last week said that GEC will "also play a supervisory role on a basis agreed with the main board of the new company". GEC will be paid for its services.

This arrangement is different in name from that which the government considered earlier this year when there was talk of awarding a management contract to someone like GEC. It is, however, unlikely to prove different in practice. Mr Tom Boardman, giving evidence to the Select Committee on Science and Technology this week, made it plain that GEC will provide the management of the new company which is to have a two tier structure. The chief board will be appointed jointly by GEC and the government. It in turn will appoint a managing board to actually run the new company.

The new £10 million organization will be chaired by Lord Aldington, GEC's deputy chairman, with Lord McFadzean, currently chairman of British Insulated Callendar's Cables as deputy chairman. A chief executive has yet to be appointed. Although existing companies in the nuclear design and construction industry can buy into the shareholding company that, with GEC and the government, will own the new company, they will not be able to directly influence the management.

This reorganization, which follows the announcement made last August that the nuclear power industry was to be concentrated in one bloc, is the first stage in ending the uncertainty that has hung over the industry for the past two years. Later this month Mr Walker is expected to announce the membership of the Nuclear Power Board which will advise him on the choice of reactor system. Its membership is expected to include representatives from the UKAEA, the Central Electricity Generating Board, the Electricity Council and government scientists.

Mr Walker told the Commons that the consultations that have taken place over

Sir Arnold Weinstock

the past six months "have confirmed strongly the government's view that there should be a single nuclear company which will use the skills and experience of the existing industry".

The radical differences between the new company and the old consortia (British Nuclear Design and Construction and The Nuclear Power Group) will be that the new company will have a single strong management, and will be responsible only for the design and construction of the nuclear steam supply systems—in other words the reactor itself. Turbogenerators and other plant will be supplied by other contractors.

Although the government will only have a 15 per cent holding in the new company it will retain "special rights in certain matters where the public interest is closely involved", Mr Walker said. "These would include the formation of international links and securing that an open purchasing policy is pursued in order that neither the company's shareholders nor GEC subsidiaries should obtain preferential treatment."

The existing work of the nuclear consortia will be taken over by the new company "under arrangements to be agreed". The position of British Nuclear Fuels in the new set up is not entirely clear. Mr. Walker said that the fuel company "will be closely associated with the new company in marketing and exploiting reactor systems and their fuel", but its precise relationship has not yet been defined. Mr Boardman told the select committee that a joint marketing company may be formed by BNFL and the new company.

Although the new organization is expected to begin operations soon, and although the Nuclear Power Board should convene and produce its advice for Mr Walker comparatively quickly, new nuclear power station orders are unlikely before next year.

US/USSR

All Aboard the Glomar

THE Soviet Union is to collaborate with the United States in a deep sea drilling project using the Glomar Challenger. This latest development in Soviet–United States cooperation follows last May's open ended agreement on scientific cooperation (see also page 294).

The Soviet Union has been interested in sea bed exploration for some time, and the current five-year plan (see *Pravda*, February 14, 1971) provides support for such projects. Until now, however, these have only involved offshore exploration for oil and minerals in the Caspian and Black Seas and on the eastern coast of the Soviet Union.

Under the new agreement the Soviet Union will contribute $1 million a year (ten per cent of the total cost) to the Deep Sea Drilling Project, and Soviet scientists will have facilities for further research work carried out by the Glomar Challenger.

To date the Deep Sea Drilling Project has been based on JOIDES, a consortium of five United States oceanographic institutions. Under the new agreement the Institute of Oceanology of the Soviet Academy of Sciences will represent the Soviet Union as the sixth member of the consortium.

Although new collaborative projects are planned under last May's agreemnt, some of which, for example, the Bering Meteorological project (see *Nature*, **241**, 420; 1973) have already taken place, this entry of the Soviet Union into existing United States work seems an unprecedented move by the Soviet planners. Soviet scientists have, however, shown considerable interest in the voyages of the Glomar Challenger for some time, and regular reports of her movements and findings have appeared in *Priorda*.

POPULATION

Government Involvement

GOVERNMENTS can not afford to dissociate themselves from population questions, according to the *Report of the Population Panel* published last week (HMSO, Cmnd 5258, 90p). The panel adds that "public opinion demands, and the facts of the population situation require, that the Government defines its attitude to questions concerning the level and rate of increase of population". The government should also, says the panel, indicate the extent to which population issues influence its policies and its choice of priorities.

By coming out in favour of the government being involved in population matters the panel echoes the sentiments of the Select Committee on Science and Technology which produced a report on population in 1971 that was the starting point for the present report.

But the panel reports that a "population policy is not a panacea for curing the ills of contemporary society". Those who suggest this, says the panel, are diverting attention from serious problems and the action needed to tackle them. The panel points out that "pressure on the countryside, congestion, social tensions, individual stress and alienation" will be serious problems whether the population of Britain is 55 million, as at present, or 70 million, which according to the latest report of the Government Actuary (see *Nature*, **240**, 173; 1972) it is not now likely to be before the middle of the twenty-first century.

Population affairs should be a ministerial responsibility, says the panel, but there is insufficient knowledge of population trends and their causes and implications for a population policy to be formulated at present. To provide more information the panel recommends that a census be carried out in 1976, five years before the next planned one, and that censuses in future should be held regularly once every five years.

To provide more demographic information the panel recommends that a centre for population studies be set up at a university. The centre should be closely allied with other departments—economics, social sciences, biology and medicine being the ones specifically mentioned.

One of the great barriers to making accurate estimates of population is a lack of knowledge of how fertility rates change. In particular there is little knowledge of how fertility varies with social class and with where the mother lives in Britain. The panel calls for research in this area and it also points out that the effects of divorce and re-

marriage on fertility are little understood.

There has also not been anything approaching a national survey on the effectiveness of contraceptive techniques although the work by the Universities of Hull and York in the city of Hull is well known. There is also a need for more research into the relationship of abortion and sterilization to fertility.

The second area, which the panel pinpoints as being in need of research is mortality and it points out that the factors affecting the death rate are largely unknown, especially for children. There is also little knowledge of why the death rate in Britain changes from region to region. There is a need for more information on the death rate simply so that more accurate predictions of the age structure of the population can be made.

The panel also says that there is need for research into the effects of both emigration and immigration, especially now that entry to the European Economic Community has, in principle, made it easier for Europeans to live in Britain and for the British to live in Europe.

The panel also points to the need for correlating fertility with IQ and other variables for which suitable tests exist or can be developed. Such tests should be carried out at regular intervals in order to detect trends.

To coordinate research and information on population, and also to provide information for the minister, the panel recommends that a small group be set up in the Cabinet Office to advise on population matters and that a committee be set up of representatives from all government departments under the chairmanship of the head of the Cabinet Office group. The terms of reference of the group would require it to determine priorities within the population field.

As a further boost to demographic research the panel recommends that the Office of Population Censuses and Surveys should be expanded and strengthened both for the analysis of demographic data from censuses and other sources and for survey work on motivation and family planning. OPCS should also commission research and should be the vehicle which disseminates information and interpretative comment on population trends.

Perhaps the recommendation of the panel which has caused most comment in the past week is that comprehensive family planning services should be provided as an integral part of the National Health Service "so that everyone knows of their existence and is free to use them". The government announced on Monday that contraceptives will be available to all on the same basis as drugs and appliances from April 1, 1974. In this respect contraceptives will not be

free—except for those that qualify for normal exemptions from prescription charges—and the estimated cost to the National Health Service will be £13 million, which is £3 million less than it would be if no charges are imposed.

CANCER RESEARCH

ICRF Spending Rises

EXPENDITURE by the Imperial Cancer Research Fund last year reached £2.7 million, £0.9 million of which went on capital developments at the fund's chief research centres at Lincoln's Inn Fields and Mill Hill (ICRF Annual Report).

The extension of the Lincoln's Inn Fields' building was finally completed late in 1972, a year behind schedule, providing the fund with an extra 41,000 square feet of space.

The year also saw the opening of the fund's medical oncology unit at St Bartholomew's Hospital with the intention of investigating how the various treatments for cancer, particularly chemotherapy and immunotherapy, can best be used, and discovering whether recent work on immunotherapy in animals can be applied to man.

The unit's current work includes attempts to lengthen periods of complete remission in patients with leukaemia and work on detecting relapses before they are clinically apparent.

The breast cancer unit at Guy's Hospital was closed last year, two years after it opened, in order to enlarge the two storey building by adding a floor ; when the unit reopens in July 1973, 36 beds will be available instead of the original 21. The unit is also planning a large prospective cancer study on women in south east London. This follow's the unit's study of 5,000 women in Guernsey which has been running since 1961 and has confirmed that abnormalities of androgen excretion are found in a high proportion of women who subsequently develop breast cancer. The unit is also comparing all aspects of breast cancer in Britain and Japan. This study, which is being carried out in collaboration with the National Cancer Centre, Tokyo, could produce some interesting results because breast cancer is very rare in Japan.

Clinical trials of ICRF 159, the drug that the fund has developed which appears to be effective against secondary tumours, have begun in the United States and in Britain, chiefly at Westminster Hospital. It is too early yet for any firm conclusions to be drawn as the trials have only been running for six months, but Dr Kurt Hellmann, head of the fund's chemotherapy unit, said this week that the first results "look very encouraging".

ICRF raised £1.7 million during 1972, an increase of £0.12 million over

1971. Of the £1.8 million current expenditure during the past year, £0.9 million was spent on research staff salaries, £130,000 on new equipment, and £214,000 on laboratory upkeep and materials.

ICELANDIC SCIENCE

Need for Expansion

ICELAND spends 0.39 per cent of its Gross National Product on research and development, a much smaller percentage than that in most other western countries, and the country's expenditure on research and development has only increased very slowly since 1950 when it ran at 0.17 per cent of the GNP (*Reviews of National Science Policy, Iceland,* OECD, Paris).

Research in Iceland is funded mostly by the government, which provides more than 70 per cent of the money, with industry running a poor second with 17 per cent of the research funding to its credit. In all, in 1971, 187.7 million Icelandic kroner (£79 million) was spent on research and development which was allocated as follows: Kr42.8 million on basic and unspecified research, Kr41.6 million on argricultural research, Kr67.4 million on fisheries research, Kr41.6 million on agricultural and construction, Kr24.3 million on energy research and Kr4.7 million on medical research. In 1966, by comparison, the total spent was Kr72.7 million and the greatest increase between 1966 and 1971 was in spending on fisheries research which went up from Kr20.6 million to Kr67.4 million.

The OECD examining team, consisting of Dr Alexander King, the Director General for Scientific Affairs at the OECD and Dr R. Major, the director of the Norwegian Council for Scientific and Industrial Research, has strong criticisms of the organization of research in Iceland. They say that the resources available for research are inadequate and that the absolute resources devoted to science "seems less than the critical amount necessary for a modern society".

Iceland has one university, and during 1970–71, 1,640 students were registered. But more than 700 Icelanders were studying abroad. Only 260 engineers and science students were registered at the University of Iceland in 1970–71 but a number of scientists were also studying abroad. Drs King and Major call for a further development of the Department of Technology and Science at the university which apart from redressing the balance of science students will form a nucleus for fundamental research "which should be oriented towards the specific natural conditions and national needs in Iceland". To overcome the difficulties of building up this department it is suggested that the staff of the Icelandic applied research institutes be involved in teaching in the university.

The National Research Council of Iceland was formed in 1940 and is the only body in the country charged with handling scientific matters on a broad basis. Iceland has no minister for science, and scientific affairs are dealt with separately by each ministry. The National Research Council is, at present, attached to the Ministry of Education but the examiners suggest that the council should be attached in future to the Prime Minister's office and also that it should be considerably strengthened by altering its membership with a view to making it a more active organization. The NRC, say the examiners, should take the initiative to create strategies and long-range plans for research activities "harmonized to the national goals of the country".

The examiners also suggest that the Icelandic applied science institutes should continue to report to their ministries but that they should strengthen their contacts with the users of their work and they also recommend that industry should be encouraged to undertake research projects. Very little research is undertaken in industry at present and this is "in the long run an unhealthy situation".

But the final words of advice from Dr King and Dr Major are that, apart from insufficient resources, the "main obstacle to the progress in science in Iceland appears to be the lack of communication and open dialogue".

CIBA FOUNDATION

Fostering Relations

THE Ciba Foundation, which exists to promote international cooperation in medical and chemical research, spent £160,000 in 1972 and sponsored no fewer than thirteen symposia at its London headquarters in Portland Place, as well as holding several smaller meetings and discussions.

The foundation was set up in 1947 by CIBA Ltd and is now financed by that company's successor, CIBA-Geigy Ltd. Each year a third of the foundation's funds come from the parent company in Basle, a third from its subsidiary in Britain and a third from subsidiaries in the United States, Canada and Mexico among other countries.

Broadly speaking 50 per cent of the expenditure each year is for scientific purposes, 30 per cent for the maintenance of the "house",—in which, among other things, accommodation is provided free for scientists visiting Britain on business—and 20 per cent on administration. Although the lion's share of the scientific expenditure is on conferences and so on, the foundation does spend on average about £1,200 a year on its Anglo-French medical exchange bursaries, which allow young French and English scientists to interchange countries for a month or two. The foundation's annual report published recently lists nine bursaries—eight to British scientists—for 1972–73.

The Ciba Foundation also spends about £500 a year on associateships at the Royal Society of Medicine; this allows about twenty foreign students a year to make use of the facilities of the society without becoming full members.

Among the symposia held by the foundation in 1972 were ones on locomotion of tissue cells, corneal graft failures, and the medical care and protection of prisoners and other detainees.

New job for Berrill?

SIR KENNETH BERRILL, chairman of the University Grants Committee, is being tipped to become the government's Chief Economic Adviser later this year in succession to Sir Donald MacDougall. The Treasury was unable to confirm this week that his appointment is imminent, but Sir Kenneth, who is a product of the London School of Economics and Trinity College, Cambridge, and who was a lecturer in economics at Cambridge from 1949–69, has both experience as a government adviser and a reputation as an extremely able administrator.

Sir Kenneth became Chairman of the University Grants Committee in 1969 and is due to retire this year; from 1967–69 he was special adviser to the Treasury, and he has also been an economic adviser to Turkey, British Guiana and the OECD.

NEW WORLD

Commission at Odds with Nixon's Drug Policy

by our Washington Correspondent

PRESIDENT NIXON was told last week that official responses to the problem of drug abuse in the United States have led to ill-defined but lavishly funded programmes, that a drug abuse/industrial complex has built up which has a vested interest in perpetuating the problem and that basic assumptions about the nature of drug abuse and its causes need to be reexamined. He was also again told that criminal sanctions against those who possess marihuana should be removed and that the rhetoric about drug abuse which constantly pours from government officials and legislators is counterproductive.

Such statements, not surprisingly, met with a cool reception from the White House, for only a week previously, President Nixon had been indulging in some high-flown rhetoric of his own, telling Congress that his Administration was making some progress in the fight against drug addiction, proposing fresh draconian legal sanctions against drug traffickers and restating his opposition to decriminalizing the use of marihuana.

The complaints about attitudes toward drug abuse and about responses to the problem came from the National Commission on Marihuana and Drug Abuse, a commission set up by Congress and charged with the task of examining the nature, causes and scope of drug abuse in the United States. If the commission's findings and recommendations are surprising, they are made even more so by the fact that nine of its thirteen members were appointed directly by President Nixon and that it was headed by Raymond P. Shafer, former Republican Governor of Pennsylvania, and not noted for liberal leanings. They were contained in the commission's second and final report, a long, closely argued document which opens up a window on the whole subject of the use and misuse of drugs and lets some welcome fresh air blow in.

The report* is an attempt to deflate emotions, cut through the rhetoric and examine the basic issues which surround drug abuse and its causes. Although the commission put forward some relatively far-reaching proposals, its chief effect will probably be to help provide an atmosphere in which official responses to drug use (the commission

*Drug Abuse in America: Problem in Perspective, available from the US Government Printing Office, Washington DC 20402, $2.60. Stock No 5266-00003.

cautions strongly against the use of words such as drug abuse and drug addiction) can be more rationally formulated. Its first report, which was published a year ago and which dealt just with the use of marihuana, similarly adopted a low-key approach, argued that the emotionalism surrounding the use of marihuana was partly responsible for its widespread use and recommended that criminal sanctions against the possession of small quantities of the drug should be removed.

The commission argues that although attention is usually focused on the opiates, and in particular on heroin, "alcohol dependence is without question the most serious drug problem" in the United States, and that addiction to

barbiturates is a more hidden problem, the dimensions of which are perhaps equivalent to the hidden opiate problem of the late nineteenth century. There are reckoned, for example, to be 9 million alcoholics in the United States. Society's attitudes towards the use of various drugs are, the commission suggests, inconsistent with respect to the costs of irresponsible use, both to society and to the individual.

Seen in terms of such costs, the commission suggests that social concern should concentrate on alcohol and heroin, that there should be moderate concern about the use of amphetamines, barbiturates, hallucinogens and cocaine and that marihuana and so-called minor tranquillizers merit the least social con-

JUPITER

Off to Jupiter Again

by our Washington Correspondent

THE second spacecraft to pay a visit to Jupiter, Pioneer G, will be launched from Cape Kennedy next week — weather and technical difficulties permitting. If all goes well it should reach Jupiter in December 1974, exactly a year after its predecessor, Pioneer 10, which was launched in March last year and which has now covered three quarters of the distance to the planet. Exactly what Pioneer G will do when it makes its rendezvous with Jupiter is still open to question, however, and will depend in large part on the results obtained by Pioneer 10.

One of the chief factors which will determine the nature of the mission is the intensity of the radiation trapped in belts around Jupiter. Some theories suggest that the intensity in the radiation belts may be about a million times stronger than in the Van Allen belts around the Earth, and it would destroy the instruments aboard a spacecraft which flies too close to Jupiter.

Before Pioneer 10 was launched, there was a strong argument for taking the spacecraft in as close to the surface as possible, so that the intensity of the radiation belts could be mapped, and so that data obtained from near the surface could be relayed back until the instruments ceased to function. It was finally decided, however, to take Pioneer 10 in to about three Jupiter radii from the centre of the planet, where the radiation should not endanger the spacecraft.

According to Mr. Charles F. Hall, the project manager, measurements taken by Pioneer 10 can be extrapolated to determine the radiation intensity closer to Jupiter, and a meeting of those who have experiments aboard Pioneer G will be called early next year to plan the mission in the light of those measurements. Mid-course corrections will then be made to the trajectory of Pioneer G (which will be renamed Pioneer 11 after launch) to alter its closeness of approach and its path past Jupiter. After the encounter with the planet, both spacecraft will eventually leave the solar system.

If the radiation intensity is not as great as some fear, and if there is sufficient thruster gas left on the spacecraft for mid-course corrections, the trajectory of Pioneer G could be altered so that it would swing past Jupiter at a distance of about half a Jupiter radius from the cloud tops, and go on to an encounter with Saturn in 1980. That would require the spacecraft to pass across the face of the planet, however, rather than behind it, and that would not be the best course from the point of view of some of the experiments. There is also a possibility of taking a look at some of the moons of Jupiter. Pioneer 10 will pass behind Io, for example, when it will be possible to tell from the effect on the radio signals whether the satellite has an atmosphere.

At least one uncertainty has been reduced by the data already sent back by Pioneer 10. The spacecraft recently completed passage through the asteroid belt and it found fewer large particles in the belt than most estimates predicted.

cern at present.

In short, the commission believes that society should adopt what can best be described as a public health policy towards the use of drugs. Arguing that the rationale behind federal, state and local programmes designed to prevent abuse and to treat and rehabilitate so-called drug abusers needs careful re-examination, the commission suggests that law enforcement, information and education, treatment and rehabilitation and scientific research all have important parts to play. But in each of these areas, present policies and attitudes leave much to be desired.

As for law enforcement, the commission believes that federal efforts, which are split between the Customs Bureau and a sheaf of agencies in the Department of Justice, are badly co-ordinated. It suggests also that a vigorous enforcement effort should be directed at middle and upper level traffickers, rather than at street level pushers, but argues strongly against minimum mandatory sentences. This is in sharp contradiction to proposals sent to Congress by President Nixon just a few days before the report was published. President Nixon called for jailing anybody convicted of selling small quantities opiates for 5 years, for a minimum of ten years in prison for those convicted of selling larger amounts, and for life imprisonment without parole for second offenders convicted of selling more than four ounces of an opiate. Mandatory minimum sentences, the commission believes, would be counter-productive, for in many cases judges may be more ready to acquit an offender rather than to lock him up and throw away the key.

The commission agonizes over the question of whether or not simple possession of an illegal drug should constitute a crime, and finally decides that only in the case of marihuana should criminal sanctions against possession be lifted. It comes to such a conclusion for two chief reasons. First, removal of criminal sanctions for possession of an illegal drug may also remove some discouragement of its use, and second, enforcement of the possession laws will help to detect persons who may benefit from treatment. Following from that, the commission recommends that a drug-dependent person arrested for an offence related to his dependence should be put into a treatment programme either in lieu of prosecution, or after conviction but before sentencing. Failure to comply with the conditions of treatment would result in return to court for conviction or for sentencing.

As for treatment, the commission believes that money has been poured into programmes with little evaluation of their effectiveness and concludes that "fundamental assumptions are not ques-

tioned, programs are not evaluated and the problem is perpetuated from fiscal year to fiscal year. 'Drug abuse' spending in the last decade can be summarized thus: an ill-defined problem emotionally expressed, led to ill-defined programs, lavishly funded."

On methadone maintenance for heroin-dependent persons, the commission suggests that it "is a promising means of neutralizing the opiate-dependent person's preoccupation with the drug. Provided drug-free regimens are also available as alternative treatment modalities, in every community, and voluntary entry is emphasized, we believe that treatment officials should continue to expand and improve maintenance services".

But the commission does decide to recommend against a heroin maintenance scheme such as the British method. If the objective is simply to reduce drug-related crime, then a heroin maintenance scheme would be appropriate, but the commission suggests that heroin maintenance schemes would tend to displace methadone maintenance, that the benefits to the dependent person are outweighed by the therapeutic disadvantages, and that in any case, other treatment methods have not yet been given a fair chance. Nevertheless, the

commission believes that the British heroin maintenance scheme should be carefully evaluated.

The report also has harsh words to say about drug information and education programmes, suggesting that they have not been properly evaluated, that many present factually incorrect material, and that some may even lead to increased use of dangerous drugs. The commission is consequently driven to recommend that an immediate moratorium be placed on the production and dissemination of new drug information materials until standards for accuracy and concept can be drawn up, and that in view of the ignorance about the impact of drug education, a moratorium should be placed on drug education programmes in schools. At the very least, the commission recommends that state laws requiring compulsory drug education classes in schools should be repealed.

Perhaps the commission's chief recommendation, directed at the federal government, is that a single, independent federal agency should be established, on the lines of the Atomic Energy Commission, to establish, coordinate and administer all government drug policy. The agency, which could be called the Controlled Substances

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EARTHQUAKES

Quake-waiting

by our Washington Correspondent

THE first official prediction that an earthquake will take place at a specific location was made last week by the US Geological Survey. There is a "good likelihood", the survey said, that a small earthquake of magnitude about 4.5 and with a focal depth of about 3.5 miles will occur at a point on the San Andreas fault about 20 miles south-east of Hollister, a small town in northern California. The only parameter which cannot be predicted so precisely is the timing—the event is expected to occur "within the next few months". Officials in the Geological Survey are quick to point out, however, that a unique and well documented set of events has led to the prediction and that other regions of the fault may not be so predictable.

In short, the earthquake is expected to take place at 36°40'N and 121°17'NE, on a segment of the San Andreas Fault which has been extensively studied by seismologists from the USGS research centre at Menlo Park. Four earthquakes of magnitudes between 4.0 and 5.0 have taken place at opposite ends of a 12.5 mile section of the fault since December 1971—two at the northern and two at the southern end—and these have increased the strain at the centre

of the section. The strain would be relieved by an earthquake of magnitude about 4.5.

Chiefly the work of two USGS seismologists, Robert L. Wesson and William L. Ellsworth, the prediction is contained in a paper which will be delivered at the annual meeting of the American Geophysical Union in Washington DC in April. The Geological Survey, anxious to allay any fears that may have arisen in Hollister after the prediction was picked up by the press last week, rushed out an announcement.

Another paper by Wesson and Ellsworth to be delivered at the AGU meeting gives details of a study of several earthquakes which took place in California between 1952 and 1972. In every case, they found that the quake was preceded by great numbers of microearthquakes, and they suggest that such activity "is a necessary condition for the later occurrence of a moderate or larger earthquake in California".

One result of the public anouncement of the prediction is that there will probably be a rush of seismologists to the area of the predicted earthquake, and the event, if it takes place, will be very carefully studied. In particular, any precursors will be closely monitored, and much valuable data could result. If it does not occur, at least the USGS has the letout that it did not predict the time of occurrence.

Agency, would absorb the functions of agencies concerned with drug abuse law enforcement, treatment and rehabilitation, research and education. To avoid institutionalizing the drug problem, the commission also recommends that the agency should be disbanded after five years. Such a drastic step is recommended because there is considerable duplication between the various agencies and little effective coordination,

Last year a Special Action Office for Drug Abuse Prevention (SAODAP) was established in the White House to oversee and coordinate the work of the various agencies concerned with treatment, rehabilitation and education programmes. But the commission suggests that the office is at best a stop-gap measure, and it has failed to provide adequate coordination. And, on the law enforcement side, the report gives details of overlap, rivalry and lack of cooperation between the various drug abuse law enforcement agencies.

The Controlled Substances Agency would distribute and monitor grants to states for treatment, rehabilitation, prevention, education and law enforcement programmes, it would develop and implement a general research plan, it would evaluate ongoing programmes and it would provide a data bank for policy planning. Like the AEC, the head of the agency would be a subcabinet official who would report directly to the President.

But the proposal has little chance of being adopted. For one thing, Senator Jacob Javits and Senator Harold Hughes, the two Senate appointees on the commission, both dissented from the recommendation because they believe that the Special Action Office has not yet been given a chance to show its mettle. Their lack of support probably precludes passage of legislation by Congress to set up such an agency. More important, a few hours after the commission's report was made public, a White House press spokesman announced that President Nixon will soon send Congress a reorganization plan to amalgamate all the drug abuse law enforcement agencies into a single agency within the Department of Justice. Although that would fit in with the commission's desire to coordinate law enforcement activities, it leaves aside the treatment, information and research activities. But the reorganization would neatly cut the ground from under the commission's feet.

In sum, the commission's report is likely to find that its chief impact will stem not from its recommendations but from its appeal for a more rational approach from its low-key assessments of prevailing attitudes as well as from the emergence of such radical suggestions from such a relatively conservative body.

INTERNATIONAL COOPERATION

Cooperation Begins

by our Washington Correspondent

COOPERATION between the United States and the Soviet Union on a number of scientific projects, promised in an agreement signed during President Nixon's visit to Moscow nearly a year ago, finally got under way last week. The US–USSR Joint Commission on Scientific and Technical Cooperation, set up by the Moscow agreement (see *Nature*, **237**, 247; 1972), held its first meeting in Washington and approved about twenty-five specific joint projects. Although the projects nearly all involve applied science and will ultimately be of benefit to industry, many of them will be carried out in universities. Approval was also given for Soviet participation in the US Deep Sea drilling Project (see page 289).

In addition to approving projects, the Joint Commission also designated specific individuals in each country to organize and coordinate the work involved in each project, and drew up guidelines for financing them. No funding levels have, however, been proposed.

In addition to the general agreement on scientific and technical cooperation, agreements on health research, environmental science and space research were also signed in Moscow last May. These other specific agreements have already produced results—putative human cancer viruses and drugs have been exchanged, a list of projects in environmental science has been agreed to, planning is progressing well on the joint Apollo-Soyuz docking mission and there has been much East-West travel by scientists and officials. And now that the Joint Commission has finally met— its first meeting has been put back several times since it was first due to take place last October—it is hoped that this new scientific detente will be extended to cover a number of new areas.

The commission agreed to proposals for joint research and development in six chief areas: energy research and development, application of computers to management, agricultural research, microbiological synthesis, chemical catalysis and water resources. The industrial bent of most of the projects is evident from the following examples in each area:

● In energy research, the commission decided to concentrate on five areas— electric power systems and transmission lines, including superconducting transmission, magnetohydrodynamics and solar and geothermal energy. Last year, when the agreement was first signed, thermonuclear research was widely canvassed as a possibility for joint coopera-

tion, but has since been dropped, possibly for security reasons.

● Systems analysis, the use of computers for managing large cities, econometric modelling and the design of software were agreed to as projects for cooperation in the field of the application of computers to management. Dr H. Guyford Stever, director of the National Science Foundation and the US cochairman of the commission, said last week that strategic products which are embargoed for export from the United States to the Soviet Union, which includes computers, were not discussed.

● In agricultural research, crop breeding and protection, increased production of farm animals and poultry and the mechanization of agricultural production were agreed as priority areas.

● On water resources, the commission approved four projects for immediate implementation — water resource planning, cold weather construction techniques, automation and remote control of water resource systems, and the use of plastics in construction.

● In the area of chemical catalysis, the commission approved five projects, including the application of catalysis to life support systems for possible use in space exploration and the use of catalysis for environment control—the use of catalytic converters for reducing harmful emissions from automobile exhausts, for example.

● Finally, on microbiological synthesis, the commission decided that a group of scientists from the United States should visit the Soviet Union before priority areas were defined.

Short Notes

Honing the Knife

ALTHOUGH Senator William Proxmire's views on economy in federal spending are by now well known, his utterances on the space budget bear especially close watching this year because he has recently been made chairman of the Appropriations subcommittee which deals with NASA's budget. Proxmire has now suggested that the agency's proposed budget for 1974 should be cut by a further $500 million, chiefly by scrapping the shuttle and stretching out the Skylab programme. The suggestion formed part of a counterbudget in which Proxmire outlined reductions of more than $4,000 million in President Nixon's spending proposals for 1974, chiefly by taking the axe to several programmes of the Department of Defense. Apart from the shuttle and Skylab, Proxmire suggests that "additional savings could be made in a much more vigorous effort to substitute unmanned for manned space efforts".

NEWS AND VIEWS

Global Perspectives on Climate

THE realization during the first four decades of this century that global climates are subject to change has been followed by a large and increasing scientific activity aimed at describing the magnitude and extent of these changes. Coupled with this, the early interest shown in the subject by planners in agriculture, industry and government has developed into an outright demand that climatic forecasts be made a few years or even decades ahead. Any attempt at prediction based solely on local climatic experience will, however, tend to founder, for the underlying secular patterns of global climatic change have a tendency to affect local climate in a radical and unpredictable way, often altering the local climate beyond past experience.

During the past twenty years these essential global patterns of climatic variation have been emerging with increasing clarity from a large accumulation of local climatic records. It is now fairly well established that from the eighteenth century until the 1920s the global atmospheric circulation, including the principal momentum-carrying winds of both hemispheres, showed a remarkably uniform tendency towards intensification ; as Mitchell and others have shown, this was accompanied by a warming of the global atmosphere, especially at high latitudes (*Proc. Rome Symp., Changes of Climate* (UNESCO and WMO), 161 ; UNESCO, Paris, 1963). There is some evidence for attributing this to an increase in the effective supply of solar energy, partly through an increase in the strength of the direct solar beam and partly through a reduction in the amount of volcanic dust in the stratosphere from the 1820s onwards. Early records of cyclone and anticyclone tracks in the Atlantic sector of the Northern Hemisphere suggest that this strengthening circulation was also accompanied by a contraction of the circumpolar vortex, a poleward shift of the axes of zonal winds and pressure belts and a lengthening of wavelengths in the upper westerlies. By the early 1930s, the Iceland Low lay further north on average than at any other time in this century and the more frequent invasion of the Arctic by depressions is held at least partly responsible for the well-known retreat of Arctic Sea ice during the 1920s and 1930s. Since then (more especially since the 1940s) this situation has been reversed with remarkable suddenness. A rapid decrease in atmospheric vigour has been accompanied by a cooling of the global atmosphere, a retraction of winds and pressure belts towards the equator, a decrease of wavelengths in the upper westerlies (at least in the Northern Hemisphere) and a record southward advance of sea ice in the European sub-Arctic. Perhaps the most plausible basic explanation is an apparent decrease in the intensity of the solar beam since the 1940s, which has been noted by several climatologists.

Whether or not the causes of these important climatic events have been correctly identified, their fundamental economic and social effects have become abundantly clear. During the present period of meridional global circulation the specific tendency over the European Arctic and sub-Arctic seas has been towards northerly meridionality and climatic deterioration. To give examples from this small sector alone, the increased northerly airflow has been held responsible directly or indirectly for the extension of sea ice to the north Icelandic coast, for a drastic and economically important alteration in the annual spawning migration of the Atlanto-Scandian herring stock to Iceland and for delaying the spring production of phytoplankton in the southern Norwegian Sea. Further, Lamb (*Nature*, **223**, 1209 ; 1969) has noted a two-week shortening of the average growing season in England since 1950, compared with the warmest decades of this century. Such fundamental changes could also be described for other sectors of the hemisphere, notably those areas where an expanding population is extending agriculture to marginal lands.

The full recognition of the economic importance of these changes together with the realization of man's increasing ability to modify climate himself (whether knowingly or unknowingly) have given the chief impetus to the present search for the tendencies, causes and global interconnexions of prominent climatic events. Observational techniques, computer technology and model making of the whole atmosphere-ocean system have advanced to support this search. From the outset, however, it is apparent that the course of this research must, at least for the present, be governed by the virtual impossibility of producing true forecasts of long-term climatic events which may be acyclic in character and may last so long that there are no analogues within the short time span covered by climatic records. A more fruitful approach lies, first, in the use of powerful modern techniques of observation and analysis to monitor the principal climatic events as they occur and, second, in the determination of the likely cause and effect relationships that will follow the establishment of a given large-scale climatic anomaly. The work of Starr and Oort described on page 310 of this issue of *Nature* represents the former category of research, set against and confirming the known tendencies of global climate and providing an insight into the type of analysis which will be some day routine. The novelty of their approach lies in the remarkable scale of the work involved. From the General Circulation Library of the Massachusetts Institute of Technology, some 150 to 200 thousand individual observations were integrated to produce each of the sixty monthly mean values which describe the temperature of the bulk (92 per cent) of the atmospheric mass in the Northern Hemisphere between 1958 and 1963. The mean water vapour content of the same atmospheric mass was computed for the same period. The downward trends which are shown in the temperature and humidity of the hemisphere are unequivocal but are, as the authors admit, so steep as to make a long continuation of the trend seem unlikely. Perhaps a future extension of this mammoth analysis will show this trend to be part of a stepwise cooling similar to that which is emerging from studies of the Arctic.

The second line of research nowadays—that of investigating the chains of cause and effect which make up global patterns of climate—is no less impressive in scope.

Sawyer of the Meteorological Office, Bracknell, has already observed that as friction and viscosity are capable of dissipating the total kinetic energy of the atmosphere in about 5 days, the cause of persistent circulation anomalies is unlikely to lie in the dynamic inertia of the circulation (*Tech. Note Wld Met. Org.*, No. 66, 227; 1965). In keeping with his conclusion that anomalies in the temperature of the sea surface are the most important single influence on weather in the long term, much work on persistent circulation anomalies is now centred on the feedback effects of ocean and atmosphere. The elucidation of these effects has been overwhelmingly the result of the work of Namias and Bjerknes in the United States, and the current NORPAX Pacific experiment represents, to a large extent, the culmination of their efforts.   R. R. D.

Insect Virus Transmission

ANIMAL virologists have long been envious of insect virologists for their ability to produce milligram amounts of purified virus with the aid of only a centrifuge and a few caterpillars. Envy is rapidly replaced by a feeling of relief, however, when the animal virologist learns of the technical problems encountered in handling insect tissue culture. Many virologists are, therefore, unaware of the uses to which insect virologists have put their knowledge, particularly in the field of insect pest control.

Apart from relative ease of propagation, insect viruses have a number of properties which make them particularly suitable for use as insecticides. Many of them are rapidly lethal to their hosts, but can be sufficiently specific in host range to leave parasites and predators unaffected. Those which cause the formation of inclusion bodies within infected cells are particularly easy to purify because these bodies, which contain infectious virus particles, are resistant to putrefaction. Thus infected hosts can be resuspended in water, allowed to disintegrate and pure preparations of inclusion bodies can be obtained by the simple procedure of differential centrifugation. These inclusion bodies are large enough to be counted in an ordinary bacterial counting chamber. Dried inclusions are very stable and infectivity persists for long periods in such preparations stored at room temperature. The viruses can, of course, multiply in their hosts and spread to insects unaffected by the initial application. These and other favourable properties have, not surprisingly, stimulated much interest, and field trials, with promising results, have been reported. Before large scale use of these viruses in the field becomes commonplace, however, several problems remain to be overcome, and the article by Longworth, Robertson, Tinsley, Rowlands and Brown on page 314 of this issue of *Nature* illustrates one of these—uncertainty concerning host range within and outside the class Insecta —in a particularly interesting way.

Dramatic control of larval populations of the moth *Gonometa podocarpi* (Lepidoptera: Lasiocampidae) in Uganda has been obtained using a virus which grows in the cytoplasm of larval gut and fat body cells (without forming inclusion bodies). The morphological, biophysical and biochemical properties of this virus closely resemble those of vertebrate picornaviruses and this caused Longworth *et al.* to examine the relationships of the *Gono-*

meta virus to selected animal picornaviruses by immunological techniques. Not surprisingly, no serological relationship between the insect and animal viruses could be demonstrated, but, unexpectedly, precipitating activity in gel diffusion tests with *Gonometa* virus was found to be present in the sera of all pigs examined. Studies on the nature of this activity showed that it was sensitive to 2-mercaptoethanol and that it sedimented in the 19S region of sucrose density gradients. Electrophoresis in agarose and electron microscopy confirmed that the precipitating activity was in fact IgM antibody. No activity was found in the IgG fraction of any serum. Subsequent testing showed antibody against *Gonometa* virus to be present in sera from cattle, sheep, horses, dogs and three species of deer, although no reactions were obtained with sera from guinea-pigs and rabbits reared for laboratory use, with wild rabbits, or with gnotobiotic pigs and cattle.

Longworth *et al.* suggest that the presence of this antibody in British animals may follow their repeated exposure to small amounts of antigen—rather than virus multiplication, explaining the lack of IgG antibody—but point out that at present *Gonometa* virus is only known to occur in an insect indigenous to East Africa and unknown elsewhere. They also point out, however, that only a small number of insects have been examined virologically and suggest that their observations indicate the existence of a virus closely related antigenically to *Gonometa* virus in a host, possibly an arthropod, in the United Kingdom and which regularly reaches mammalian hosts. The authors conclude that the apparent regular transmission of such viruses to mammalian hosts highlights the potential risks arising from the deliberate release of viruses to control insects should the viruses show a wider host range than expected.

None of the viruses studied by insect pathologists has as yet been found to multiply in a non-insect host, though it should be remembered that arboviruses, traditionally studied by animal virologists and classified as animal viruses, multiply—by definition—in both their vertebrate hosts and in their arthropod vectors, and that many viruses pathogenic for plants also multiply in their arthropod vectors. The observations of Longworth *et al.* thus serve to stress the necessity, already apparent on general grounds, of thorough testing of any potential viral insecticide for safety to humans, livestock, wild life and crops.
                                               T. H. P.

Transport of Excitons?

WHEN light in the visible or ultraviolet part of the spectrum is absorbed in a solid, the photon is converted into an excitation of the atoms. It is a very important feature of some electronic excitations that they can be transferred very efficiently from atom to atom and that energy can thus be transported away from an illuminated surface. Such processes are important in fields as diverse as power generation, photography and biosynthesis. Although these concepts of energy transfer can be elaborated theoretically, it is not at all easy to detect this transfer and identify the mode precisely. In the absorption spectrum of a semiconductor or dielectric, one of the most intense absorptions is at an energy slightly less than that of the forbidden energy gap. The theory is that a

photon at this energy is converted into an excited pair consisting of an electron and a hole. The electron and the hole do not drift apart but stay bound to each other. They are not, however, too tightly bound to the parent atom. They represent packets of energy which can, in theory, drift through the network of atoms by means of a very efficient quantum mechanical transfer or "resonant transfer" of energy (Dexter and Knox, *Excitons*, Wiley; 1969). The importance of the exciton configuration is the high level of stored energy (say 6 eV for an alkali halide) and the theoretically long time before recombination.

Although the lifetime of an exciton is expected to be long in an ideal solid lattice, it may be limited to a few nanoseconds in a typical real solid by surfaces and lattice defects; a typical diffusion range is much less than a millimetre. It is, however, difficult to find where an exciton started its life and where it was annihilated. No current flows and no track is left. One is obliged to try to observe the effects of the energy released at annihilation and to eliminate the possibility of other forms of energy transport from the region where the light was absorbed. Several attempts have been made to measure the exciton diffusion length in cadmium sulphide. For example, Broser and Balkanski (*Z. Elektrochem.*, **61**, 715; 1957) illuminated a crystal with a fine spot of light and found that this could produce an electric current between two electrodes in a different region. The migration of energy could, however, possibly be accounted for by absorption and re-emission of light. Another important energy transfer process involving excitons was proposed in a satisfying new model for the formation of F-centres in alkali halides (Pooley, *Proc. Phys. Soc.*, **87**, 245, 257; 1966; Hersh, *Phys. Rev.*, **148**, 928; 1966). In this model, kinetic energy from an exciton annihilation is used to start a focused collision sequence in a crystal which ends with the expulsion of a halogen atom into an interstitial site. Townsend (*Phys. Lett.*, **28A**, 587; 1969) elegantly confirmed that ion motion is indeed involved when he showed that illuminating a very clean crystal of potassium iodide with light in the first-exciton band could produce efficient sputtering. An elaboration of these experiments has now unexpectedly produced an observa-

tion which could be interpreted as exciton motion; the method has more elegance and is probably less ambiguous than earlier experiments.

Al-Jammal, Pooley and Townsend (*J. Phys. C.*, **6**, 247; 1973) recently found that an electron beam of energy of several hundred electron volts gave a surprisingly high sputtering yield in potassium iodide, with an unexpected maximum in the curve of efficiency against energy occurring at 400 eV. This result implies that energy is being transported efficiently to the surface through 25 nm of crystal (the stopping range for 400 eV electrons). Most probably the transport is excitonic. The efficiency is so high that fluorescence and reabsorption are unlikely. Focused collision sequences are again known to be much too inefficient; for example, if 5 eV of kinetic energy is imparted to one atom, at least 1 eV is lost in transferring that energy to the next atom and so on down a chain of atoms. Five stages of transfer would be completed within only 5 nm. Alternatively, interstitial atom diffusion is possible but the effects of thallium ion doping are stronger than would be expected according to this explanation. Thus one is left with exciton diffusion as the most likely mechanism.

Using some approximations to esti-

mate the profile of electron energy deposition, Al-Jammal *et al.* estimate the exciton diffusion length to be about 20 nm. Probabilities of resonant transfer in KI are such that an exciton should jump once every 10^{-13} s on average. For three-dimensional diffusion, the estimated typical range, 20 nm, will be achieved if the exciton lifetime is 2×10^{-8} s. This is of the same order of magnitude as the lifetime estimated by Collins (*J. Appl. Phys.*, **30**, 1135; 1959) and Bleil and Broser (*J. Phys. Chem. Solids*, **25**, 11; 1964) for excitons in cadmium sulphide. Thus a fairly consistent picture emerges. It has been shown that defects serve as traps and recombination centres for excitons in many materials. Thallium in potassium iodide acts in this way and was used in this experiment to check the consistency of the exciton diffusion model. Measurements on a crystal doped with thallium showed a reduced diffusion length of only 13 nm. This result gives a trapping cross-section for the thallium ion which fits well with its ionic radius.

The novelty of the approach derives from the use of a surface phenomenon, namely sputtering, to measure energy release in the lattice, rather than fluorescence, which was used in most of the previous experiments.

A.G.H-S.

Transfer RNAs and Tumour Viruses

RNA tumour virus particles, in addition to containing 60–70S RNA which is presumably the viral genome, contain 4S RNA molecules that have been shown to be transfer RNAs specified by the host cell in which the virus particles matured. Furthermore, it is known that the relative amounts of various species of tRNAs in the virus particles and in the host cells differ, which suggests that the tRNAs in the virions are not simply a representative sample of the tRNAs in the host cell. It is not known why RNA tumour virus particles carry tRNAs, or how they get into the virions during maturation, but in *Nature New Biology* next Wednesday (April 4) Wang *et al.* describe some experiments which indicate that the viral genome may somehow control which species of tRNAs are incorporated.

Wang *et al.* compared the tRNA populations in non-defective avian sarcoma virus particles, SR.RSV, in avian leucosis virus particles, RAV.1, and in Bryan high titre Rous sarcoma virus particles grown in the presence of

RAV.1, which acts as a helper for the replication of the defective Bryan virus to yield phenotypically mixed BH.RSV (RAV.1) particles. They found that the relative amounts and number of species of tRNAs in RAV.1 and BH.RSV (RAV.1) particles differ and that the tRNAs in SR.RSV particles resemble those in BH.RSV(RAV.1) particles. The RAV.1 particles contain not only absolutely more chargeable tRNA molecules than either sarcoma virus but also more species of tRNAs. The pattern of tRNAs in transformed and untransformed chick cells was, however, very similar.

It seems, therefore, that leucosis viruses and sarcoma viruses propagated in the same cells pick up different populations of tRNAs and therefore that the viral genome may exert some control over this incorporation. What part if any the tRNAs play in the life cycle of the viruses still remains to be elucidated, but these experiments do suggest the incorporation of tRNAs is more than a chance event.

CHROMOSOMES
Model of *X* Inactivation

from a Correspondent

THE most interesting explanation yet proposed for the mechanism of *X* chromosome inactivation in mammals has been put forward by Brown and Chandra (*Proc. US Nat. Acad. Sci.,* **70,** 195 ; 1973). The chief problem in considering *X* chromosome inactivation is to envisage a mechanism which will lead one whole chromosome of an apparently similar pair to become inactive in somatic cells, while the other retains its normal genetic responsiveness. A step forward came with the discovery that in certain marsupials the inactive *X* is always of paternal origin (Sharman, *Nature,* **230,** 231 ; 1971 ; Cooper *et al., Nature New Biology,* **230,** 154 ; 1971). This led Cooper (*Nature,* **230,** 292 ; 1971) to postulate that the random inactivation of maternal or paternal *X* chromosomes in eutherian mammals has evolved from an earlier simpler system of paternal *X* inactivation.

Although it is still far from clear whether inactivation of paternal *X* is in fact the general rule in marsupials, Cooper's idea is attractive because the sex chromosomes, and indeed the chromatin generally, do seem to become inactive during spermatogenesis ; thus, if the paternal *X* remains inactive in the new zygote, this would seem a simpler system than if it were reactivated, and this followed by a random inactivation. In detail, however, Cooper's model contained difficulties and grounds for criticism (Lyon, *Biol. Rev.,* **47,** 1 ; 1971).

Brown and Chandra's model incorporates the idea of evolution from an ancestral inactivation of paternal *X*, but eliminates many of the difficulties. Basically, they propose a system of two genes controlling the activity of the *X* chromosome ; one, sensitive to parental origin, acts on the second, the receptor, which determines the activity of the *X* chromosome. In marsupials, they suggest, both these genes are located on the *X*, so that if an *X* passes through a male gamete its sensitive gene is inactive, and its receptor gene is never activated. During evolution, they next suggest, the transfer of the sensitive gene to an autosome led to *X* inactivation at random in eutherians. Eutherians thus have an autosomal pair of sensitive genes, of which only the one of maternal origin is active. This gene produces "a single informational entity that attaches to a receptor site on one of the *X* chromosomes encountered at random". In other words, the number of active *X* chromosomes in a eutherian is equal to the number of maternally-derived autosomal sensitive genes.

Such a model fits well with many known facts concerning *X* inactivation. In individuals with chromosome anoma-

lies, if the number of autosomes remains normal, then no more than one *X* chromosome should remain active no matter how many are present and what their parental origin. This is indeed what is observed, even in 2*A* : *XXXXY* or 2*A* : *XXXXX* individuals. Conversely, if the number of autosomes is disturbed, as in triploids or tetraploids, then the number of active *X* chromosomes should depend on the number of maternal sets of autosomes. In particular triploids could have either two maternal and one paternal set, or one maternal and two paternal, and so should be of two types, with two or one active *X* chromosome(s). This again is observed. Tetraploids, if formed by doubling of chromosomes of an originally diploid zygote, should have two active *X* chromosomes, as indeed they do. The piece of evidence which is least well explained by the model is the preferential non-random inactivities of human *X* chromosomes with deletions. But because the non-randomness in this case could be the result of cell selection rather than disturbance of the inactivation mechanisms, this point is not important.

Thus Brown and Chandra's hypothesis has elegance, simplicity and is in principle eminently testable. Individuals with anomalies of the relevant autosome should have alterations of *X* chromosome activity and the type of alteration will depend on the parental origin of the anomalous chromosomes.

If the model proves to be correct, it will be the first clear instance in mammals of the activity of single alleles in autosomes, except for the immunoglobulins which could be a special case. Nucleolar-organizing regions are sometimes found on only one of an autosomal pair. This might fit with Comings's suggestion (*Amer. J. Hum. Genet.,* **20,** 440 ; 1968) that active and inactive *X* chromosomes are distinguished by their site of attachment in the nucleus, if a nucleolus rather than the nuclear membrane is the critical site of attachment (Lyon, *Nature New Biology,* **232,** 229 ; 1971). The active *X* chromosome would be attached to the same nucleolus as the maternal autosome.

One virtue of Comings's model is that it eliminates the need for the unidentified "information entity" which Brown and Chandra postulate, and which does pose something of a difficulty because it must be some unit substance, which can activate only one receptor site. Another general difficulty, met by all models of *X* inactivation proposed so far, is that of explaining how one complete chromosome is activated or inactivated, rather than just a short region. Brown and Chandra's model offers nothing new on this point, hence it has the further endearing quality that, if it should be proved right, there will still be intriguing problems left to tackle.

MYOSIN
Amputating Heads

from our Molecular Biology Correspondent

THE myosin molecule gives the impression of a protein designed by an international committee of protein chemists. It is a chimaera of globular and fibrous parts, contains chains of very high and of low molecular weight, and has complex enzymatic and ligand-binding properties. The long two-stranded α-helical shaft forms part of the lattice of the thick filaments of the myofibril, and the globular heads project out of the filament axis. During the contractile process, when these heads interact with the actin of the thin filaments, their angular orientation changes, but it is by no means clear how this very sizable change in geometry is accomplished. The vague notion of a hinge at some point in the shaft has often enough been invoked, but the evidence in favour of such a region in a superwound double α-helix, behaving hydrodynamically as a rigid rod, has been at best exiguous. There remains, however, the high specificity of tryptic cleavage of the shaft, which occurs about one-third of the way from the end that bears the two globular heads. This has always suggested to the more febrile minds in the field a rather loosely organized segment, or dislocation, in this region. Burke, Himmelfarb and Harrington (*Biochemistry,* **12,** 701 ; 1973) have now given more tangible expression to such a view.

They have examined the properties of the entire myosin shaft, which can be prepared by shearing off the heads with papain. The time course of hydrolysis of these rods with trypsin can be fitted by three rate processes differing over nearly two orders of magnitude in their apparent velocity constants. The fastest process is presumed to be associated with hydrolysis in a uniquely labile region. Next, thermal melting profiles, in which the diminution of α-helical structure with increasing temperature is followed by means of optical rotation, show clear evidence of biphasicity, with one transition below and another above about 50° C. After digestion through the rapid hydrolysis phase and part of the slower phase, the resulting light meromyosin, comprising the terminal two-thirds or so of the shaft, shows only a single cooperative melting transition. Moreover, below this sharp transition the viscosity of the light meromyosin is invariant with temperature, whereas that of the intact rod falls markedly with increasing temperature even before the first optical transition.

The authors infer from all this that there is in the myosin rod a sizable region of α-helix, which melts more readily than the rest, is relatively flexible and in consequence readily attacked by

proteases. Such a weakly structured region, they hazard, might respond to an applied tension by uncoiling. This extended form will resist any further tension, and might be expected to annihilate it by a condensation process. Burke *et al.* interpret in these terms the biphasic change of tension in a muscle subjected to a rapid change in length, which was recently described by Huxley and Simmons. They have attempted to induce a change in the tendency of the rod to distort by addition of contraction-linked ligands, such as ATP, ADP, and calcium and magnesium ions, though without success.

The indications are that the other α-helical muscle proteins, in particular the molluscan paramyosins, which have no globular heads, are very similar in most important structural respects to the myosin rod, and Halsey and Harrington (*ibid.*, 693) have undertaken a parallel study on clam paramyosin. As with myosin rods, tryptic hydrolysis displays a very rapid initial phase in which a labile region is destroyed. A "light meromyosin" is generated, which melts thermally in a single transition, corresponding to the higher of two transitions observed in the melting of the intact paramyosin. The amino-acid compositions of the two parts of the molecule differ and that of the surviving rod has a higher computed α-helix-forming potential (at least by criteria drawn from analysis of globular protein conformations); indeed the composition of the material released in the early stages of trypsin hydrolysis should in these terms be distinctly unfavourable for the stability of α-helices. This lends support to the possibility of a region of distorted, or at least weakened, α-helix in this molecule. Cowgill in a report last year also showed evidence of two regions in the molecule differing in stability, the stable "light meromyosin" being the N-terminal end.

As to the question of whether and why two heads are in fact better than one, Margossian and Lowey (*J. Mol. Biol.*, **74**, 301 ; 1973) have set out in search of an answer by preparing, by papain treatment under highly selective conditions, followed by ion-exchange chromatography, one-headed myosin, as well as one-headed heavy meromyosin. Properties such as molecular weights and α-helix contents coincide nicely with the expected values, and the fragments contain their complements of light chains. The mutilated molecules look exactly as they should in the electron microscope. In the accompanying article (*ibid.*, 313), which has all the attributes of a definitive utterance, Margossian and Lowey compare the functional properties of the one and two-headed species as well as isolated heads with no shaft (subfragment-1). The ATPase turnover of the two-headed

protein is, as nearly as it is possible to estimate, twice that of the one-headed derivatives, which indicates the self sufficiency, and to a first approximation independence, of the two heads. The actin-binding stoichiometry, measured with the ultracentrifuge, is one actin subunit per head, in agreement with recent work of Eisenberg and co-workers, and in contradiction of earlier results of Young. A somewhat tortured analysis of the behaviour of unfractionated mixtures of partially inactivated myosins by Toikawa and Morales not long ago led them to the conclusion that both heads of myosin must be operative for superprecipitation with actin. Margossian and Lowey have been able to consign this notion to limbo by showing that their one-headed myosin when mixed with F actin superprecipitates very nicely. Only the time lag is longer, and this may be put down to the greater affinity with which the two-headed species would be expected to interact with the F actin.

The problem of why myosin need have two heads is still unanswered, leaving only some enigmatic fragments of evidence against their precise equivalence. Anybody with a serious interest in the field will want to study the analysis

given by Margossian and Lowey of ATPase activity in relation to actin binding, which goes some way towards clarifying a situation obfuscated by stratum upon stratum of hypothesis.

Galapagos Endemics

from our Plant Ecology Correspondent

IN 1971 Wiggins and Porter published a new *Flora of the Galapagos Islands* (Stanford University Press. California) which has provided the raw material and the necessary incentive for the initiation of more extensive research into the flora of these islands. Johnson and Raven (*Science, 179*, 893; 1973) have subjected the data from this *Flora* to rigorous statistical and phytogeographical analysis.

Only 26 per cent of the Galapagos flora is endemic, a figure which compares poorly with the Hawaiian Islands where more than 90 per cent of the vascular plant species are endemic. The percentage of endemics in the individual floras of the Galapagos Islands is inversely related to the area of the islands, a situation which can be explained by reference to the pattern of

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A Persistent Cell Population in the Thymus

THE thymus in the centuries following its first description was regarded as a mysterious organ. Many and bizarre were the functions ascribed to it until the works of Miller and of Good showed that it regulated the development of immunological responsiveness —at least in some species of mammals. Since then it has been revealed that the thymus performs this function by liberation of what have come to be known as T lymphocytes. Much emphasis has been placed by cellular immunologists on this versatile species of cell and its more productive ally (as far as antibodies are concerned), the B lymphocyte. But, aside from its capacity for producing cells, the thymus itself has retained much of its mystery. It is suspected to emit a hormone, but hardly anything is known of the process of differentiation whereby the organ gives rise to T cells. In next Wednesday's *Nature New Biology* (April 4) Elliott deals with heterogeneity of cells within the thymus.

It is usually accepted that after treatment of a mouse with corticosteroids, such as hydrocortisone, there remains in the thymus, after much cell death, a population of steroid-resistant cells. In an earlier report, Elliott *et al.* (*Nature New Biology,* **234**, 77; 1971) showed that these cells were not T cells that had come in from outside the organ but were cells that were in the thymus

at the time of treatment with corticosteroid.

The method involved the engraftment of a chromosomally-marked but otherwise syngeneic thymus graft into a normal mouse and then, after treatment with hydrocortisone, display of the phytohaemagglutinin (PHA)-responsive cells from the graft *in vitro*. Elliott now extends this observation and shows that with or without treatment with hydrocortisone most of the cells in a thymus graft at any time after its emplacement, that can be induced to respond to PHA, are cells that are native to the graft.

The thymus is usually thought of as a staging house through which pass stem cells and their mitotically amplified products. In a thymus graft active mitosis of the native cells in the graft itself ceases by about the twentieth day after grafting and yet, as Elliott shows, many weeks later the PHA-responsive cell population revealed *in vitro* contains many of the native cells which previously would have been assumed to have emigrated to the periphery.

The functional significance of this persistent cell population is not known nor is the morphology of the persistent cell. Immunologists who think of thymocytes as equivalent to peripheral T cells should, however, remember that they are also handling a cell population which never seems to leave the thymus.

vegetation types in the islands. There are three basic zones of vegetation. The littoral zone has a high rate of plant immigration, but also a high rate of extinction. Here there are few endemic species. Lowland areas, which are particularly extensive in the Galapagos and are arid, are rich in endemics. Elevated areas have a moister climate and a low proportion of endemic species. Because the larger islands are also those which possess the regions of greatest altitude, it is to be expected that island areas will be negatively correlated with the proportion of endemics in the flora.

The reason for the frequency of endemics in the arid zone and their scarcity in the moist uplands is probably to be found in the climatic history of the Galapagos Islands. Colinvaux has found (*Nature*, **240**, 17; 1972) that the wet climate of the uplands dates back only 10,000 years. Arid climates, however, have existed on the Galapagos for at least 34,000 years and probably for much longer than this. Long established taxa are therefore liable to be adapted to arid conditions.

Some species of the moist, elevated areas, however, are endemic, for example, the tree *Scalesia pedunculata* and the shrub *Miconia robinsoniana.* Concern about the future of plants such as these on the Galapagos is expressed by E. K. Schofield (*Biol. Conserv.,* **5**, 48 ; 1973). Because the uplands receive most of the available rainfall, it is these areas which are subjected to the most intensive cultivation by the 3,000 human occupants of the islands. Not only does this involve the physical clearance of natural vegetation, but it has also resulted in the spread of exotic species introduced by man. Many of these exotics, such as *Phlox* and *Ricinus,* seem to be spreading from the disturbed areas into the natural plant communities. It is widely recognized that island faunas are particularly sensitive to the introduction of non-native species and undoubtedly the same is true of plants, though this is less well documented. It is to be hoped that an adequate conservation policy will be introduced into the Galapagos before irreparable harm ensues and the extinction of endemic plant species results.

PESTICIDES
Atmospheric Distribution

from a Correspondent

THE factors which affect the distribution of pesticides throughout the atmosphere were discussed by members of the Physicochemical and Biophysical Panel and the Pesticides Group of the Society of Chemical Industry at a symposium held on March 6 at the society's rooms in London.

Dr R. A. E. Galley (Chairman of the

Pesticides Group) reviewed the factors which cause pesticides to enter the atmosphere. Vaporization can occur from falling spray particles and from plant, water and soil surfaces. Transport by winds can occur over very large distances and the vapours can be deposited onto the Earth's surface in rain water. Although the concentrations of organochlorine particles in air or rain water are usually between 1 and 20 parts in 10^{12} the first mile of the atmosphere could contain up to 8,000 tons of these pesticides.

Dr C. A. Edwards (Rothamsted Experimental Station, Harpenden) considered that the high rates of loss of pesticides from soils often observed soon after application might be explained by volatilization. He said that this process had received relatively little consideration in the past but there are signs that it is beginning to receive more attention now. Dr F. T. Philips (Rothamsted Experimental Station, Harpenden) described his work on the volatilization of pesticides from glass and plant surfaces, from which it was clear that the interaction of adsorption, wind speed, crystal size and temperature is very complex.

Dr D. A. M. Watkins (Long Ashton Research Station, Bristol) discussed the implication of the vapour phase photochemical decomposition of pesticides. It is known that many pesticides are decomposed by short wavelength radiation and it was pointed out that although the spectrum of radiant energy which reaches the Earth's surface is very narrow, photochemical reactions could play an important part in degrading pesticides which had diffused to the upper atmosphere.

The global transport of pesticides by birds was the theme of the talk by Dr P. R. Evans (University of Durham). A recent estimate suggests that 5,000 million song birds migrate from Europe and Siberia to Africa south of the Sahara each year. About 1,500 million die in Africa, thereby depositing pesticide residues which originated in northern latitudes. Calculations show that 7–11 kg of DDT is transported in this way each year.

Professor R. S. Scorer (Imperial College, London) suggested that the current philosophy of spraying crops to protect them from insect pests is highly inefficient and analogous to spraying human beings to protect them from malaria. He said that pests must be controlled on a regional international basis and that this would enable meteorologically-induced macro swarms to be tracked down and attacked. Much more biological knowledge of the life cycle of insects is required and this has to be related to a whole range of scientific disciplines. This contribution aroused a great deal of controversy but its concepts were well supported by radar photographs which showed that very many species of insect do in fact occur in large numbers in the atmosphere.

Further support for Professor Scorer's suggestion came from Dr R. C. Rainey (Centre for Overseas Pest Research) who described the way in which meteorological conditions have been used to enhance the distribution of pesticides when applied by ultra low volume techniques. He quoted the highly efficient controls of desert locust and African army worm that have been obtained by the use of dieldrin.

Induced Replication of Satellite DNA

WHEN mouse cells in culture replicate their DNA prior to mitosis, the satellite DNA fraction of the cell genome, which is defined by its comparatively simple base sequence, is replicated late in the S phase of the cell cycle after the bulk of the non-repetitive DNA has replicated. It is not surprising therefore that considerable interest was aroused in 1970 by Smith, who reported that when baby mouse kidney cells are infected by polyoma virus, satellite DNA replicates early in the S phase before the remainder of the DNA.

This observation by Smith seemed to indicate that polyoma virus somehow alters the sequence in which different fractions of the cell genome are replicated, an observation with many implications for models of DNA replication in mammalian cells. Unfortunately, however, as Hatfield and Walker report in *Nature New Biology* next Wednesday

(April 4), Smith's results are not "readily reproducible".

Hatfield and Walker, as a preliminary to further investigating this phenomenon, decided to repeat Smith's experiments keeping conditions as close as possible to those he used. They obtained polyoma virus from Smith, for example, and then used it to infect confluent cultures of non-dividing baby mouse kidney cells. Infection resulted in a stimulation of cell DNA synthesis, but in eleven experiments Hatfield and Walker failed to detect preferential early replication of light satellite DNA.

There seems to be no satisfactory way of reconciling Smith's results with those of Hatfield and Walker, and the latter group is forced to the conclusion that the time of replication of satellite DNA in these mouse cells, stimulated to divide by being infected by polyoma virus or by being exposed to serum, is similar.

TUMOUR VIRUSES

Viral Proteins

from our Cell Biology Correspondent

WHEN simian virus (SV) 40 infects and transforms non-permissive cells—cells which do not support replication of the viral genome—the SV40 DNA becomes integrated into the DNA of a host chromosome(s). Usually the whole viral genome must be integrated because SV40 can be rescued from cells of most clones of transformants by fusing them with permissive monkey cells. Furthermore, the integrated viral genome is transcribed in the transformed cell, even though it is not replicated independently of host chromosomes, because viral RNA can be detected in the nucleus and cytoplasm. Presumably these viral RNA transcripts act as messengers for those proteins which cause transformation.

Obviously tumour virologists would dearly like to isolate the transformation-inducing viral proteins; that hard task remains to be done, but considerable progress has been made towards analysing the pattern of transcription of the integrated viral genome. This is technically easier to do, of course, because the two strands of the viral DNA can be separated and specifically fragmented to yield probes specific for viral RNA sequences. Khoury and Martin and their colleagues at the National Institutes of Health (Khoury et al., J. Virol., 11, 54; 1973), for example, have reported an analysis of the SV40 RNA made in eleven clones of SV40 transformed cells of various species (mouse, human, sheep, rat and hamster). In nine of these eleven clones the cells contain RNA transcribed from 37 to 50 per cent of the strand of SV40 DNA that is transcribed at early times during the replication of the virus in permissive monkey cells. In two other clones the cells contained transcripts corresponding to 65-75 per cent of this early or minus strand of the SV40 DNA. It seems therefore that in transformed cells all the SV40 early genes are transcribed, together with variable amounts of the early strand DNA not transcribed in permissive cells. In nine of the eleven clones the cells contained no detectable amounts of RNA transcribed from the complementary late or plus strand of the viral DNA which is transcribed after the commencement of DNA replication during the lytic cycle. It may well be therefore that in these transformed cells late genes are not transcribed at all but the possibility that the late genes are transcribed and then the transcripts are rapidly degraded has not been ruled out. In two other clones the cells contain some late RNA but it corresponds to less than 8 per cent of the late strand DNA.

These data, and similar data that have been obtained by Keller and Sambrook and were reported at the recent Lepetit meeting, rule out the possibility that the late genes of SV40 are involved in specifying transformation proteins. Either, therefore, the early genes that are also expressed during the lytic cycle specify transformation proteins or possibly anti-late RNA transcribed from segments of the early or minus strand of DNA that are not transcribed during the lytic cycle specify transforming proteins.

Because there is no clue as to the nature of the transforming gene protein(s) and because cells infected by SV40 and its close relative polyoma virus continue to make their own proteins, it is wellnigh impossible to fish out viral proteins other than capsids from infected cells. Several groups have therefore tried to identify viral proteins made in cell free systems that support coupled transcription and translation of viral DNA. Crawford and Gesteland (J. Mol. Biol., 74; 627; 1973), for instance, have programmed a coupled Escherichia coli cell free system with polyoma virus DNA and have detected the synthesis of polypeptides of various sizes including a polypeptide that corresponds in size to the major protein of the virion. Fingerprint analyses of tryptic digests of this in vitro polypep-tide indicate that it is indeed related to the major protein of the capsid, and many of the smaller polypeptides made in vitro probably correspond to incomplete capsid protein molecules. But all of the polypeptides made in vitro also contain amino-acid sequences not present in the major capsid protein made in vivo. Crawford and Gesteland conclude therefore that "The aim of characterizing all the polypeptides coded for by polyoma virus DNA and synthesized in vitro will almost certainly require the development of a more homologous system". They might also have added that even when systems which support coupled transcription and translation of polyoma DNAs are obtained from mammalian cells the task of identifying anything other than the major capsid protein will remain formidable.

The juxtaposition in the Journal of Molecular Biology of Crawford and Gesteland's article with that of Varmus et al. (ibid., 613) serves to underline the comparative ease with which tumour virus nucleic acids can these days be detected in host cells and the difficulty in detecting tumour virus proteins. Varmus et al. set out to detect the DNA proviruses of Rous sarcoma virus in four lines of mammalian cells trans-

Messenger Specific Initiation Factors in Eukaryotes

STUDIES on the translation of mammalian mRNAs in heterologous cell-free systems and in vivo in amphibian oocytes have suggested that the initiation factors required for translation of eukaryotic mRNAs are common to a large number of cell types. Globin mRNA, however, can only be translated on embryonic chick muscle ribosomes in the presence of reticulocyte initiation factor IFM$_3$ which binds mRNA to ribosomes. Does tissue specificity exist at the translational level? This is the question tackled by Wigle and Smith in next Wednesday's Nature New Biology (April 4).

Wigle and Smith used a fractionated cell-free system from Krebs II ascites cells to study the translation of a number of natural mRNAs. They isolated and purified from a ribosome-free ascites supernatant a cytoplasmic initiation factor (IF$_{EMC}$) required for the translation of encephalomyocarditis viral RNA (EMC RNA). Use of sparsomycin, which inhibits chain elongation, and examination of the initiation peptides by high voltage electrophoresis, showed that IF$_{EMC}$ is required for initiation on EMC RNA and that such initiation occurs at the correct initiation site.

IF$_{EMC}$ factor is specific for EMC RNA translation and is not required for translation of synthetic polynucleotides. Translation of globin mRNA in the fractionated ascites cell-free system is only slightly stimulated by addition of factor. Addition of another ascites cytoplasmic fraction EF-1, however, did stimulate globin synthesis, suggesting the presence of a globin initiation factor(s) in this fraction. Translation of bacteriophage MS-2 RNA in the ascites system is not stimulated by purified IF$_{EMC}$ but stimulation does occur in the presence of crude supernatant. Thus a factor(s) exists in the crude ascites supernatant which can direct the initiation and translation of MS-2 RNA.

Several other workers have detected initiation factors in the cytoplasm of eukaryotic cells but these seem to be involved in the binding of initiator tRNA to ribosomes. The results of Wigle and Smith indicate the presence in ascites cytoplasm of messenger-specific factors required for the recognition of specific natural mRNAs. If the number and relative amount of each factor vary in different tissues, this could account for the observed tissue specificity in the translation of mRNA. Thus the undifferentiated oocyte may contain many factors for the many classes of mRNA produced in early embryogenesis, whereas a more differentiated cell may have lost factors specific to classes of mRNA no longer required for its function. That the factors may not be absolutely specific is indicated by the success in translation of mRNAs in heterologous systems achieved by other workers.

formed by two strains of Rous sarcoma virus. By measuring the rate of reassociation of mixtures of denatured DNA from the transformed cells and DNA reverse transcribed from Rous sarcoma virus RNA, they have estimated that in both transformed rat and transformed mouse cells there are two genome equivalents of Rous sarcoma virus DNA per cell genome. Furthermore, this viral RNA is associated with cell DNA of high molecular weight which suggests that the proviruses are covalently integrated in cell chromosomes.

LASERS

Identifying Transitions

from a Correspondent

THE assignment of molecular infrared and ultraviolet spectra will be much assisted and the detailed knowledge of molecules much enhanced if a laser spectroscopy technique proposed by Skribanowitz, Kelly and Feld of MIT (*Phys. Rev.*, **6**, 2303; 1972) can be realized experimentally.

In general, infrared spectra result when molecules are raised from their ground state to some vibrationally excited state through the absorption of radiation and each vibrational state of a gaseous molecule has an associated set of closely-spaced rotational energy levels labelled with rotational quantum numbers, J. By virtue of simultaneous changes of rotational state during a vibrational transition, gas phase infrared spectra can exhibit a fine structure. Except for the simpler molecules, this rotational fine structure is rich, complex and often unresolved by conventional spectroscopic techniques, notwithstanding the severe restriction that only those changes of rotational quantum number, J, of -1, 0 and $+1$ between the lower and upper vibrational states (called P, Q and R branch transitions respectively) are permitted. Even if resolution is possible, the unambiguous assignment of J values to the upper and lower state of a component transition can be a difficult problem. Similar, but often more extreme, difficulties are encountered in attempts to analyse rotational substructure of electronic spectra in the visible and ultraviolet regions.

The group at MIT propose a simple technique to solve the assignment problem while simultaneously taking care of resolution difficulties. The necessary requirements are that two component transitions A and B of the fine structure of, for example, a vibrational band share a common rotational level in the upper state and that A exceeds B in frequency. A high powered, monochromatic laser (called the pump), of such frequency and power both to induce molecules to undergo transition A and to saturate it, acts on a low pressure gas. Molecules

in the gas have a spread of velocities, given by the Maxwell-Boltzmann distribution, relative to the direction of the incident radiation and therefore the wavelength at which they absorb the radiation will be shifted by the Doppler effect to different extents by different molecules, leading to the so-called Doppler broadened absorption profile for the transition. On account of the laser monochromaticity and the sharpness of molecular energy levels in a low pressure gas, however, only molecules within a tiny velocity range can be excited to the common upper state, for all other molecular velocities shift the incident wavelength away from resonance.

If a low powered laser beam, collinear with the pump, is now tuned over the absorption profile of transition B, the selective increase in population of the shared upper level manifests itself as a decrease in absorption (called the change signal) in a narrow region of the Doppler broadened absorption curve of B. The two crucial properties of the change signal are its sharpness and the symmetrical structure it exhibits when (but only when) A exceeds B in frequency. The sharpness ensures high resolution, and the number, spacing and relative intensity of the symmetrical components reveal the J values to be assigned to the levels involved in transitions A and B.

The reasons for the structure of the change signal and its usefulness in spectral assignment are readily understood. In the absence of an external

field a molecular rotational state of quantum number J is really the superposition of $(2J+1)$ substates of identical energy, each labelled by one of the sub-quantum numbers $M=J$, $J-1$, . . . 0, . . . $-J$. When the pump and probe laser beams are polarized in parallel directions, transitions A and B only occur between states of the same M and therefore the initial three-level system is actually the superposition of several independent three-level subsystems, each characterized by a different value of M. Under the influence of the saturating pump laser, the change signal associated with a given subsystem M splits into a symmetrical doublet whose separation depends only on the magnitude of M, the values of J for transition A and the laser field strength. Thus, each subsystem produces a doublet of different splitting and the total change signal is clearly a set of symmetrical peaks with a common centre.

The MIT group thoroughly discuss the structure of the change signal as an aid to spectral assignment and in particular they show how relative intensities among the subsystem doublets depend both on M and on the three J values involved in the transitions A and B. Distinctively different patterns can occur for the various possible combinations of transition type (P, Q or R branch) for A and B. The number of components in the change signal is, of course, another clue to the values of J, for the doublet splittings are indepen-

Surface Properties of Lymphocytes

THERE is an increasing number of ways of describing lymphoid cells. Two reports in next Wednesday's *Nature New Biology* (April 4) by Rowe *et al.* and by Lippman offer two more such methods.

Surface-bound immunoglobulins have been known to characterize a proportion of normal peripheral blood lymphocytes in both mice and men for some time. Immunoglobulins of all classes have been described and there is evidence for both immunoglobulin class restriction on some cells and lack of such restriction on others. The result obtained tends to depend on the method of demonstration. It is usually supposed that immunoglobulin-bearing lymphocytes are B cells of bone-marrow origin and that their surface globulins are receptors which facilitate the production of antibody by the cells which bear them. Rowe and his colleagues make the observation that a high percentage of lymphocytes (14 per cent) from human cord blood carry IgD on their surface, whereas adult humans have only four per cent of their lymphocytes so coated. The significance of this observation, which has been made in two different centres, is obscure as is the functional significance of IgD itself.

Lippman describes measurements of steroid binding protein (SBP) on various populations of human peripheral blood lymphocytes from normal persons and from those with various kinds of leukaemia. The method is a competitive binding assay using radioactive steroids *in vitro* on a cytosol preparation. It is shown how the SBP levels of lymphocytes from patients with acute lymphoblastic leukaemia (ALL) can be considerably higher than those of lymphocytes from normal volunteers. In patients with ALL, who have been treated with glucocorticoids (among other chemotherapeutic agents), however, the levels of SBP were consistently lower than those of untreated patients.

The object of the study was to obtain a method for the prediction of which patients might respond to treatment with glucocorticoids—those with high SBP levels—and in this respect the work seems highly promising. There is, however, a possible spin-off for the cellular immunologists in that T (thymus-derived) and B cells might differ in their SBP levels and that this difference could relate to differences in their sensitivities to glucocorticoids.

dent of the sign of M and there are at most $(2J+1)$ subsystems of different M if J is the smallest of the values involved. Detailed line shapes for the patterns expected in the experimentally favourable cases of ammonia and hydrogen fluoride are also calculated by Skribanowitz and his colleagues, so that all that remains to be seen is whether such effects will be detected and how useful they will be for molecules of more complex and less well known spectra.

ELEMENTARY PARTICLES

Protons and Partons

from a Correspondent

THE Royal Society had a lot to contend with when it held its meeting on proton scattering at very high energies on March 8. For one thing the windows were vigorously shaken during the afternoon session by the car bomb in Whitehall, about a quarter of a mile away. It was, nevertheless, an absorbing meeting.

Three new devices have greatly extended knowledge of high energy collisions. The Russian 70 GeV/c accelerator at Serpukhov has provided precise data on elastic scattering and extensive bubble chamber data on particle production processes. The 300 to 400 GeV/c machine at the National Accelerator Laboratory (NAL) near Chicago has been running for about a year, and the first-generation experiments at the CERN intersecting storage rings (ISR) near Geneva are nearing completion. These machines take one from a laboratory beam energy of about 30 GeV, at the CERN proton synchrotron and the Brookhaven alternating gradient synchrotron, to the equivalent of about 2,000 GeV at the ISR. As Professor G. Cocconi (CERN) put it in his introductory talk, matter can now be studied at densities more than 100 times greater than the density in the nucleus, although the opportunity does not last for more than about 10^{-24} s. Only in the initial "big-bang" at the formation of a universe, or possibly in the "black hole" at the death of a large star, is such a density thought to be reached for a longer time.

Many of the data which were reported from the new machines cannot yet be explained theoretically, but there has been considerable progress since the international conference at NAL last summer. A potentially exciting suggestion comes from the ratio of positive to negative particles produced with large transverse momenta at the ISR. There is a clear excess of positive particles. The simplest explanation of this is that in the most "head-on" of proton-proton collisions, the constituent particles (or partons) which form the two protons make violent direct collisions with one

another and go off at large angles. In the commoner "peripheral" collisions the individual partons are thought to act collectively. If there are only a few partons (three, for example) in each proton, then the fact that the proton has a positive charge requires a significant excess of positive over negative partons. The parton masses are apparently very large, for they have never been observed directly, but if the underlying process is a collision of mostly positive partons, the ordinary secondary particles observed at large angles will also be more positive than negative. If the number of partons in a proton were large, say thirty, then the fact that a proton has a single unit of positive charge would only have a small effect on the relative number of positive and negative partons, and hence could not be expected to bias the observed charge at large transverse momenta. There is no satisfactory model on which to base exact calculations of the effect, but this proton-proton scattering result fits in well with data on neutrino and antineutrino scattering obtained in the Gargamelle bubble chamber at CERN. Both experiments suggest that there is a small number of partons in a proton, and it is therefore possible that the partons may be "quarks" of relatively

simple type suggested by Gell-Mann and Zweig in the early 1960s.

Another result from the ISR has allayed fears that the new machines would only probe deeper into "asymptopia", the energy region in which all measurable parameters would settle down to approach to a limiting behaviour. At Serpukhov energies, all total cross-sections seemed to be tending to a constant, but experiments at the ISR have revealed that the proton-proton cross-section goes up again by 10 per cent (see Nature, **242**, 233 ; 1973). Nobody knows why, although it may be associated with the increased range of masses available for diffraction dissociation as the energy increases. Other surprising results are the behaviour of the real part of the forward scattering amplitude, which seems to be passing through zero at the lower ISR energies but which may become positive at the highest energy, and the large numbers of particles produced with large transverse momenta. Some features of the data do agree well with previous predictions, the "scaling" behaviour of single particle distributions with energy for instance, but all the indications seem to be that a new region of physics is being opened up rather than that a predictable continuation of the old region is occurring.

Wolf-Rayet Systems and X-ray Binaries

MASSIVE X-ray binaries and Wolf-Rayet (WR) systems may represent different stages in the evolution of the same kind of object. In next Monday's Nature Physical Science (April 2) van den Heuvel lists the basic parameters of the five X-ray sources known to be associated with binary systems and compares these with parameters of nine double-lined and eclipsing WR binaries with known orbits. He argues that the large mass and intense radiation from the secondaries in the X-ray systems suggest that these are black holes or neutron stars, produced by the evolution of normal massive close binaries.

In such a system, mass is transferred from the primary to the secondary as it evolves, so that the primary becomes an almost pure helium star. The secondary grows to become a hydrogen-rich OB star, and the helium star ends its life as a type II supernova some 1.7×10^6 yr or less after the first stage of mass exchange ; the residue, now the secondary of the evolved system, is a black hole or neutron star. Further evolution of the new primary leads to mass transfer on to this object and the production of X-rays 4 to 6 $\times$ 10^6 yr after the supernova event.

This is a commonly painted picture. But van den Heuvel now points out that during part of this evolutionary pattern the system is very like a WR binary. He has calculated the final

binary periods resulting from spherically symmetric explosions of typical WR stars, assuming a remnant mass of either $M_\odot$ or 4 $M_\odot$. The test masses were chosen because the mass of the secondary in Cen X-3 is less than 0.84 $M_\odot$ and the mass of the secondary in Cyg X-1 is at least 4 M. For two known WR binaries, V 444 Cygni and CQ Cephei, these calculations indicate final periods close to those of the X-ray binaries. Four other WR systems could, it seems, evolve into X-ray binaries with periods only slightly greater than that of 2U 0900-40 (8.96 day).

The delay between supernova explosion and activity of the X-ray source is sufficient to explain why no supernova remnant is seen associated with the X-ray sources, and it is interesting that if this evolutionary model is correct then there should be X-ray binaries with periods in the range 10 to 150 day. Van den Heuvel points specifically to the source 2U 0525-06, which is relatively weak ($\sim 10^{33}$ erg s^{-1}) and has been identified with the spectroscopic binary θ^2 Orionis, which has a period of 21 day and in which the primary is not yet filling its Roche lobe.

The model is certainly attractive qualitatively, but the evolution of massive close binaries which engage in large scale mass transfer is far from being well understood quantitatively.

UNIVERSAL ISOTROPY

Essential Requirement for Life ?

by our Cosmology Correspondent

Two fundamental problems each provide common cause for discussion among cosmologists. Why is the Universe isotropic? Is the Universe bound or unbound? Now, Collins and Hawking (University of Cambridge) suggest that the isotropy of the Universe is a direct result of its expansion with a velocity just on the border between infinite expansion with more than the escape velocity and eventual collapse under the gravitational influence of the whole system. Further, they argue that galaxies can only grow in such a universe, and that therefore the presence of life is a direct consequence of the isotropy of the Universe—or at least, the two have a common cause (*Astrophys. J.*, **180**, 317 ; 1973).

To take the second common question first, the problem of the Universe being bound or unbound is simply one of the velocity of expansion of the Universe in relation to the escape velocity (throughout this discussion a big-bang origin is assumed). The amount of matter in the Universe inferred from observations of bright galaxies is not sufficient to close the system and prevent ultimate expansion to infinity. But there could well be enough dark matter—cool gas, black holes, or even neutrinos—to do the job. Because this dark matter is by definition invisible from Earth, there is plenty of scope for discussion.

Too little is known about the Universe for the discussion to be closed yet. But another topic which has now been closed for discussion is the question of the isotropy of the Universe. With the discovery of the microwave background radiation, and the growing conviction that this is indeed a relic of the big-bang, ever more sophisticated measurements have shown that the radiation, and hence the Universe, is isotropic. One of the most recent measurements, reported by Parijskij, sets as a limit that there are no fluctuations of the blackbody background above the 0.8×10^{-4} K r.m.s. level at 2.8 cm on scales of 3 arc min to 1 arc deg (*Astrophys. J. Lett.*, **180**, L47 ; 1973). The temperature of the radiation is about 2.7 K, so the accuracy of these measurements is indeed good.

Given that the Universe is isotropic, then, what can be deduced about its origin and other parameters? One difficulty which arises is that if the Universe is homogeneous and isotropic—like the Robertson–Walker model—how do local inhomogeneities such as galaxies and stars grow up? As Collins and Hawking point out, the usual way in which this problem has been tackled is by studying the growth of small perturbations in a Robertson–Walker back-

ground. But perturbations grow disappointingly slowly in a Robertson–Walker universe, and this has led, for example, to suggestions that the original state of our Universe was one of extreme chaos and irregularity. Certainly not all initial conditions would lead to a universe like the one in which we live.

Even worse, initial inhomogeneities should lead to eventual anisotropy. Collins and Hawking have tackled the problem from a different point of view, adopting the philosophy attributed to Dicke and Carter that there is not just one universe but an infinite ensemble of universes, so that all the peculiarities in which mathematicians delight can have a physical being. Only those universes which contain galaxies can have intelligent life, say Collins and Hawking, and galaxies will not occur in highly anisotropic universes.

The philosophy is supported by the mathematics. It turns out that spatially homogeneous model universes can be divided into three classes: those which expand at below the escape velocity and eventually collapse ; those which expand

at just about the escape velocity ; and those which expand with more than the escape velocity. Those in the first class do not exist long enough to become isotropic, and in any case there is probably insufficient time for galaxies to grow in them during the expansion phase. The third class do not tend towards isotropy, according to Collins and Hawking, and in any case initial perturbations will not grow in density because they too will be expanding more rapidly than the local escape velocity.

That leaves a small class of models, not unlike Robertson–Walker models, expanding at the critical escape velocity and tending towards isotropy. Only in these universes can initial perturbations grow into galaxies. As Collins and Hawking put it, the answer to the question "Why is the Universe isotropic?" is "Because we are here". That seems to be putting the cart before the horse ; I would prefer to answer the question "Why are we here?" by saying "Because the Universe is isotropic". But however one splits that particular hair, the point is that we are here, the Universe is isotropic, and that such a situation can indeed be explained with sensible cosmological assumptions.

Is Cyg X-3 Similar to Sco X-1 ?

THE Cyg X–3 radio flare "closely resembles outbursts which are frequently observed to take place in radio galaxies and quasars", write Braes *et al.* in next Monday's *Nature Physical Science* (April 2). The energies involved in this outburst from a small source within our Galaxy are, of course, several orders of magnitude less than those associated with the violent extragalactic events. But Cyg X–3 is only about 10 kpc away from Earth, and its angular size (0.01 arc s on September 24) implies an expansion velocity of 0.2 *c*. Several active extragalactic sources have shown evidence of similarly high expansion velocities, and indeed such sources often consist of at least two components. Braes *et al.* point out that it is possible that an event similar to that observed in Cyg X–3 last year could have produced the triple structure seen in the radio source associated with Sco X–1.

All this speculation arises from an analysis of detailed observations of Cyg X–3 during September and October 1972 at 1.4 and 2.7 GHz, using the Westerbork synthesis telescope and the Effelsberg 100-m instrument. The observations provide further support for the view that Cyg X–3 lies either within or behind the hydrogen emission feature at −68 km s⁻¹ (see also Lauqué *et al.*, *Nature Physical Science*, **241**, 94 ; 1973). Together with kinematic evidence, this means that the distance to the source is at least 10 ± 1.5 kpc ; the radio observa-

tions suggest that Cyg X–3 is not much further away than this.

More details of the multiple structure of the radio flare are also presented by Braes *et al.* The first event, which lasted from September 3 to 10, was a simple outburst consistent with an expanding synchrotron source. The second event was more complex and violent, with three distinct maxima. The first flare (September 3) was similar to the first component of the second event, but the second and third components of that event lasted twice as long and cannot be explained in terms of a repetition of the same process with different energies on the basis of the data available so far. It is not yet possible to say whether the longer durations are a result of smooth injection or repeated discrete injection events. Cyg X–3 now seems to have returned to its normal state.
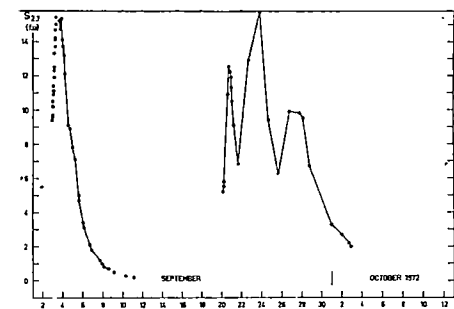
Observations of Cyg X–3 flares at 2.7 GHz with the Max Planck 100-m telescope at Effelsberg.

Mental Illness as a Metaphor

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This article is a slightly modified and expanded version of Professor Szasz's introductory remarks on the BBC television programme *Controversy*, recorded at the Royal Institution on July 27, 1972, and broadcast on October 2, 1972.

ABOUT twenty years ago I began to clarify what seemed to me the core problem of psychiatry—namely, the nature of so-called mental illness. This led to a systematic scrutiny and refutation of the two fundamental claims of contemporary psychiatrists — that mental illnesses are genuine diseases, and that psychiatry is a *bona fide* medical speciality[1,2].

It is impossible to undertake an analysis of the concept of mental illness without first coming to grips with the concept of ordinary or bodily illness. What do we mean when we say that a person is ill? We usually mean two quite different things: first, that he believes, or that his physician believes, or that they both believe, that he suffers from an abnormality or malfunctioning of his body ; and second, that he wants, or is at least willing to accept, medical help for his suffering. The term "illness" thus refers, first, to an abnormal biological condition whose existence may be claimed, truly or falsely, by patient, physician, or others ; and second, to the social role of the patient, which may be assumed or assigned.

If a person does not suffer from an abnormal biological condition, we do not usually consider him to be ill. (We certainly do not consider him to be physically ill.) And if he does not voluntarily assume the role of one who is sick, he is not usually considered to be a medical patient. This is because the practice of modern Western medicine rests on two tacit premises—namely, that the physician's task is to diagnose and treat disorders of the human body, and that he can carry out these services only with the consent of his patient. In other words, physicians are trained to treat bodily ills—not economic, moral, racial, religious, or political "ills". And they themselves (except psychiatrists) expect, and in turn are expected by their patients, to treat bodily diseases, not envy and rage, fear and folly, poverty and stupidity, and all the other miseries that beset man. Strictly speaking, then, disease or illness can affect only the body. Hence, there can be no such thing as mental illness. The term "mental illness" is a metaphor.

Origins

To understand current psychiatric practices, it is necessary to understand how and why the idea of mental illness arose and the way it now functions. In part, the concept of mental illness arose from the fact that it is possible for a person to act and to appear as if he were sick without actually having a bodily disease. How should we react to such a person? Should we treat him as if he were not ill, or as if he were ill?

Until the second half of the nineteenth century, persons who imitated illness—that is, who claimed to be sick without being able to convince their physicians that they suffered from *bona fide* illnesses—were regarded as faking illness

and were called malingerers ; and those who imitated medical practitioners—that is, who claimed to heal the sick without being able to convince medical authorities that they were *bona fide* physicians—were regarded as impostors, and were called quacks.

As a result of the influence of Charcot, Janet, and especially Freud, the perspective, both medical and lay, on imitations of illness and healing was radically transformed. Henceforth, persons who imitated illness—for example, who had "spells"—were regarded as genuinely ill, and were called hysterics ; and those who imitated physicians—for example, who "hypnotized"—were regarded as genuine healers, and were called psychotherapists. This profound conceptual transformation was both supported and reflected by an equally profound semantic transformation—one in which "spells", for example, became "seizures", and quacks became "psychoanalysts".

A few brief quotations from Freud's early writings must suffice to support my contentions. In 1893, Freud wrote that "hysteria has fairly often been credited with a faculty for simulating the most various organic nervous disorders[4]". While seeming to offer a simple description of the characteristics of the disease called "hysteria", Freud here falsifies the historical record.

Most of the contemporaries and predecessors of the young Freud credited not hysteria but malingerers with the "faculty for simulating. . . ." Indeed, being an abstraction and a name, hysteria cannot simulate or imitate anything : only persons can. Nor is this an isolated figure of speech or stylistic peculiarity of Freud's ; on the contrary, it is a part of his systematic strategy for reifying and personalizing pseudomedical labels, and for stigmatizing and depersonalizing persons. Thus, in the very same paper Freud asserts that ". . . hysteria behaves as though anatomy did not exist or as though it had no knowledge of it[5]". But hysteria neither behaves nor knows ; only persons do.

In the same year, Breuer and Freud made their now famous announcement that "hysterics suffer mainly from reminiscences"[6]. Here we are offered a metaphorical expression as if it were a literal one: for in the context in which it occurs, the statement implies that hysterics suffer from reminiscences in the same way as arteriosclerotics suffer from hardening of the arteries. But reminiscences are not real lesions ; nor, therefore, are hysterics real patients.

Lastly, in a paper published in 1909, Freud acknowledges that the hysteric fakes illness. By then hysteria was well-enough established as a legitimate illness ; and Freud did not use such direct language to say so. What he said was that ". . . (hysterical) attacks are nothing else but phantasies translated into the motor sphere, projected on to motility and portrayed in pantomime[7]". In plain English: hysteria is the dramatic imitation of illness. Nevertheless, Freud would have us believe that hysteria is itself an illness.

The upshot of this psychiatric-psychoanalytic "revolution" is that, today, it is considered shamefully uncivilized and naively unscientific to treat a person who acts or appears sick as if he were not sick. We now "know" and "realize" that such a person is sick ; that he is obviously sick ; that he is mentally sick.

But this view rests on a serious, albeit simple, error:

it rests on mistaking or confusing what is real with what is imitation; literal meaning with metaphorical meaning; medicine with morals. In other words, I maintain that mental illness is a metaphorical disease: that bodily illness stands in the same relation to mental illness as a defective television set stands to a bad television programme. Of course, the word "sick" is often used metaphorically. We call jokes "sick", economies "sick", sometimes even the whole world "sick"; but only when we call minds "sick" do we systematically mistake and strategically misinterpret metaphor for fact—and send for the doctor to "cure" the "illness". It is as if a television viewer were to send for a television engineer because he dislikes the programme he sees on the screen.

Mental Illness and Psychiatry

Such considerations lead to two diametrically opposed points of view about mental illness and psychiatry. According to the traditional and at present generally accepted view, mental illness is like any other illness; psychiatric treatment is like any other treatment; and psychiatry is like any other medical speciality. According to the view I have endeavoured to develop and clarify, however, there is, and can be, no such thing as mental illness or psychiatric treatment; the interventions now designated as "psychiatric treatment" must be clearly identified as voluntary or involuntary: voluntary interventions are things a person does for himself in an effort to change, whereas involuntary interventions are things done to him in an effort to change him against his will; and psychiatry is not a medical but a moral and political enterprise.

Whereas illness is something a patient has or claims to have or is said to have, treatment is something a physician does or claims to do. Clearly, however, not everything a physician does constitutes treatment, but only those of his interventions that are believed to be helpful or effective against the illness from which the patient suffers; and, among these, only those interventions to which the patient, assuming him to be a conscious adult, consents. In a free society, the fact that a person has an illness or that an illness is attributed to him—regardless of whether the illness is bodily or mental, literal or metaphorical—does not, and cannot, by itself justify imposing medical treatment on him against his will.

Thus, the quarantining of patients with certain contagious diseases has been justified, and can be justified, only by society's right to protect itself from the patient's illness; it cannot be justified by society's right to protect the patient from the consequences of his illness.

It is sometimes claimed that, like patients with contagious diseases, some patients with so-called mental diseases also "endanger society". The precise meaning and the factual validity of this claim are doubtful at best, and the use to which it is put, to justify the necessity of involuntary psychiatric interventions, is illogical and immoral. For if and when "mental patients" endanger or injure others, they do so not through their "illness" but through their behaviour. That this is so is self-evident: it is inherent in our very ideas of contagious and mental diseases. Contagious diseases, such as syphilis or tuberculosis, are things that not only patients can have, but also corpses; whereas mental diseases, sucn as depression or psychopathy, are things that corpses assuredly can never have. Hence, if and insofar as it is deemed that "mental patients" endanger society, society can, and ought to, protect itself from the "mentally ill" in the same way as it does from the "mentally healthy"—that is, by means of the criminal law. To be sure, society cannot do so as long as it recognizes "mental illness" as both an incriminating condition (as in involuntary hospitalization), and an excusing condition (as in the insanity defence and verdict).

In short, one of the fundamental moral and political implications of the views I have presented here is that one of our most important and most precious rights, and at present one of the most threatened, is the right to be ill— that is, the right to reject treatment, the right to suffer, and the right to die unmolested by interventions imposed upon us by the state acting through its medical (or psychiatric) agencies. In a theological society, we could not sin or die without the cleric, whether we wanted him or not. *Mutatis mutandis,* in a therapeutic society such as ours, we cannot be sick or die without the clinician, whether we want him or not[8,9].

British Examples

Lest it be thought that these considerations apply only to psychiatric conditions and practices in the United States, I should like to conclude by calling attention to several recent cases reported in the British press.

First, there are the three women who had been incarcerated in psychiatric institutions for fifty years because of illegitimate pregnancies[10-13]. Perhaps it will be objected that that was long ago, and that such things no longer happen today. Of course not. Today women are hospitalized involuntarily not for having illegitimate babies, but for having illegitimate ideas, which we conveniently call "delusions".

Second, there is the Jordanian eye doctor, the son of the Grand Mufti of Jerusalem, who was accused of killing three children, was promptly found "unfit to plead", and was "detained in a hospital"[14-16].

And third, there is the case of Graham Young, tried only a few months ago, who, having been "cured" at Broadmoor of the disease of enjoying poisoning people, had an unfortunate relapse and poisoned several more[17-20]. Revealingly, his last bout of evil, though phenomenologically undistinguishable from his previous one, was not attributed to mental disease: this time he was sent to prison, not to Broadmoor. It is difficult to imagine a more clear-cut illustration of one of my basic propositions—namely, that what we call mental illness (especially in a legal context) is not a condition, but a policy; not a fact, but a strategy; in short, not a disease that the alleged patient has, but a decision we make about how to act toward him, whether he likes it or not.

I submit that each of these cases demonstrates an insistent denial of the differences between disease and deviance; between healing for the benefit of the suffering patient and social control for the protection of society; and between medical institutions whose clients are at liberty, because they are free adults, to leave the premises should they be dissatisfied with the service, and penal institutions whose inmates, because they are convicted offenders, are deliberately and explicitly deprived of this option.

What, then, is to be done? A few simple things; however, because of our intense devotion to the medical perspective on human problems, these may prove to be quite unpalatable.

First, as so-called mental health problems are not medical but human (that is, moral, social, and political) problems, we cannot solve them by therapeutic means; we must stop continuing and even intensifying our efforts to solve them by such means.

Second, since the vocabulary of psychiatry serves to redefine systematically moral and political problems as diseases, we must repudiate and stop this abuse of our language.

Third, as psychiatric "treatments" are chiefly overtly or covertly involuntary, such interventions must be disavowed; we must reject the use of psychiatrists as policemen, judges and jailers; and we must seriously dedicate ourselves to the proposition that "mental health" workers should help only those who want to be helped, that they should do so only in ways acceptable to their clients, and that they should stop doing everything else.

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The Synthetic Chemical Literature from 1960 to 1969

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The literature of synthetic chemistry is growing at a rate of 8.7% a year—that is, doubling every 8.3 years. Data on 1.2 million compounds based on more than 128,000 abstracts published in *Index Chemicus* have been analysed. The articles abstracted contain 9.2 new compounds on average.

Current Abstracts of Chemistry and Index Chemicus is a weekly abstracting service covering published journal articles reporting primarily new chemical compounds, new reactions or new syntheses[1,2]. *Index Chemicus* (*IC*) was started in June 1960. Originally a monthly publication, *IC* became a biweekly in 1961 and a weekly in 1967. During the period of the study reported here, 1960 to 1969, all articles containing new inorganic as well as organic compounds were abstracted. The fundamental criteria for a "new" compound are, however, the author's claim of novelty, lack of a reference indicating previous publication of the compound, and therefore the presumption of novelty as for many intermediates.

This ten-year census updates an earlier five-year report[3]. It is not based on sampling. Rather, precise records have been kept for each journal. The number of articles abstracted and new compounds indexed for the calendar years 1960 to 1969 are shown in Table 1. The number of papers published each year almost tripled during this ten-year period. The first-year growth is atypical because the number of journals covered was then growing rapidly. Growth in subsequent years averaged 8.7%.

The number of compounds per abstract has stayed and remains remarkably steady at an average of 9.2 compounds an article.

By the end of 1969, records were abstracted of more than 1.2 million new compounds. By the end of the Second World War, there were approximately 1 million known chemical compounds in existence, so the new compounds reported between 1960 and 1969 are more than in the entire history of chemistry up to the end of the war. Between 1945 and 1959 another 1 million compounds were reported.

Table 2 shows the percentage of articles published in six of the chief scientific languages—English, German, Russian, French, Japanese and Italian. Ukrainian is included under the heading Russian. "Others" include Spanish, Czech, Hungarian, Polish, Rumanian and so on.

English, as the leading scientific language, has steadily been gaining in strength from 50% of the total output in 1960 to more than 61% in 1969. German, which was formerly the leading scientific language of chemistry, diminished from 17% to 10% during the same period. This does not mean a decline in scientific output by German scientists. On the contrary, the growth of research elsewhere as well as the increased use

Table 1 Compound/Abstract Ratios

Year	Abstracts	Compounds	Compounds/ abstract	Increase in No. of abstracts % yr⁻¹
1960	7,581	70,408	9.3	
1961	9,167	87,496	9.5	
1962	9,899	94,172	9.5	7.4
1963	10,838	100,623	9.3	9.5
1964	12,084	110,230	9.1	11.5
1965	12,824	119,217	9.3	6.1
1966	13,943	128,830	9.3	8.7
1967	15,275	137,245	9.0	8.1
1968	17,830	167,340	9.3	10.1
1969	19,285	172,793	8.9	8.1
Totals	128,726	1,188,354	9.2 (average)	8.7 (average)

Table 2 Language Distribution 1960–1969

Language	1960 A	1960 C	1961 A	1961 C	1962 A	1962 C	1963 A	1963 C	1964 A	1964 C	1965 A	1965 C	1966 A	1966 C	1967 A	1967 C	1968 A	1968 C	1969 A	1969 C
English	49.9	49.4	53.0	53.3	52.1	50.9	53.8	52.5	55.5	51.5	55.2	54.6	56.0	54.0	56.9	55.5	61.3	59.7	61.4	60.2
German	16.9	18.7	16.4	18.8	16.2	18.3	16.5	19.1	15.9	18.7	16.4	17.4	15.3	17.4	13.8	15.4	11.8	13.5	10.0	12.6
Russian	14.7	13.1	16.0	12.6	16.4	13.3	16.2	13.4	16.8	14.7	16.4	14.4	16.4	13.9	16.4	14.0	15.4	12.5	17.4	13.8
French	7.5	8.6	5.2	6.1	5.8	7.3	6.0	7.2	4.8	6.9	5.9	7.1	5.5	7.6	6.2	8.3	5.7	7.4	5.9	7.2
Japanese	7.0	6.2	5.7	5.3	6.5	6.0	3.5	3.2	3.1	3.6	3.0	3.1	2.9	3.4	3.1	3.4	2.3	2.9	2.9	3.0
Italian	2.4	2.9	2.0	2.6	2.0	2.6	2.4	3.4	2.1	2.9	1.8	2.3	1.7	1.9	1.9	2.3	1.6	2.2	1.1	1.6
Others	1.6	1.1	1.7	1.3	1.9	1.6	1.6	1.2	1.8	1.7	1.3	1.2	1.9	1.9	1.6	1.3	1.9	1.8	1.5	1.2

A, abstracts; C, compounds.

of English has reduced the percentage, although there was a larger number of abstracts. The same is true of Japanese, which decreased from 7% in 1960 to 2.9% in 1969 during the most spectacular period of growth in the history of Japanese industry. There are many Japanese journals published today in English, and those journals published in Japanese have extensive English summaries.

This same trend also prevails in the languages of other smaller countries—there are very few scientific articles published in Hebrew and Arabic, for example. Almost all papers from developing countries are published in English. A large percentage of Latin American papers appear in English-language journals.

This same trend is not true for articles published in the Soviet Union. Soviet scientists publish overwhelmingly in Russian with the exception of a relatively small number of articles which appear in multilingual international journals, such as *Tetrahedron, Tetrahedron Letters* or *The Collection of Czechoslovak Chemical Communications*. In these cases, Soviet scientists publish their work in English, German or French. Soviet chemical publishers are also still quite resistant to the idea of publishing English language summaries. In general, however, there has been practically no change in the percentage of Russian language publications during the past ten years. The average of 16%, although much lower than figures reported by *Chemical Abstracts* (18.4%)[4] for all fields of chemistry, is still high by comparison with Western countries. This is in part a consequence of the emphasis in the United States on physical organic rather than synthetic organic chemistry research.

Analysis by Journals

Table 3 shows the sixty top-ranking journals, as far as new chemical compounds are concerned, for 1969. It is interesting to note that eleven of the highest yielding twenty journals are published in English, and these accounted for 75% of the compounds. While many older well-established journals like the *Berichte, Annalen, Journal of the American Chemical Society*, and *Helvetica* have remained fairly stable, others like *Bull. Soc. Chim. France* have doubled in content as have the Japanese journals published in English. But the newly-established journals like *Tetrahedron Letters* and *Journal of Medi-*

Table 3 Number of New Compounds Reported in 1969

Rank	Journal title	No. of compounds	Rank	Journal title	No. of compounds	Rank	Journal title	No. of compounds
1	*J. Chem. Soc. (A, B, C)*	11,811	21	*Helv. Chim. Acta*	2,530	41	*Gazz. Chim. Ital.*	1,033
2	*J. Org. Chem.*	9,682	22	*Inorg. Chem.*	2,349	42	*Farmaco Ed. Sci.*	1,029
3	*J. Med. Chem.*	7,775	23	*J. Organometallic Chem.*	1,981	43	*Z. Anorg. Allgem. Chem.*	1,024
4	*J. Amer. Chem. Soc.*	7,638	24	*J. Heterocyclic Chem.*	1,954	44	*Roczniki Chem.*	1,001
5	*Bull. Soc. Chim. Fr.*	6,486	25	*J. Prakt. Chem.*	1,912	45	*Khim. Farm. Zh.*	997
6	*Tetrahedron Lett.*	6,272	26	*Austral. J. Chem.*	1,841	46	*Dokl. Akad. Nauk. SSSR*	961
7	*Chem. Ber.*	5,829	27	*J. Inorg. Nucl. Chem.*	1,723	47	*Arch. Pharmaz.*	945
8	*Tetrahedron*	5,525	28	*Arm. Khim. Zhur.*	1,575	48	*Arzneimittel-Forsch.*	900
9	*J. Chem. Soc. D Chem. Commun.*	5,415	29	*Zhur. Neorg. Khim.*	1,570	49	*Z. Naturforsch. B*	893
10	*Zh. Obshch. Khim.*	4,965	30	*J. Indian Chem. Soc.*	1,475	50	*Carbohyd. Res.*	769
11	*Zh. Org. Khim.*	4,398	31	*Acta Chem. Scand.*	1,407	51	*J. Chem. Soc. Jap. Pure*	751
12	*CR Acad. Sci. C.*	3,837	32	*Coll. Czech. Chem. Commun.*	1,407	52	*Ukr. Khim. Zhur.*	728
13	*Chem. Pharm. Bull. Jap.*	3,777	33	*Rec. Trav. Chim.*	1,259	53	*Biochemistry*	714
14	*Ann. Chem. Liebigs*	3,721	34	*Chim. Ther.*	1,151	54	*Rev. Roumaine Chim.*	684
15	*J. Pharm. Soc. Jap.*	3,195	35	*J. Pharm. Sci.*	1,123	55	*Khim. Prirodnykh. Soed.*	669
16	*Khim. Geterots. Soed.*	3,041	36	*Makromol. Chem.*	1,103	56	*Agr. Biol. Chem.*	662
17	*Canad. J. Chem.*	2,913	37	*J. Polymer Sci. A-1*	1,085	57	*Vysokomol. Soed. A*	660
18	*Indian J. Chem.*	2,806	38	*Angew. Chem.*	1,061	58	*J. Chromatog.*	646
19	*Bull. Chem. Soc. Jap.*	2,745	39	*J. Chem. Soc. Jap. Ind.*	1,060	59	*J. Agr. Food Chem.*	639
20	*Izvest Akad. Nauk. SSSR Khim.*	2,579	40	*Z. Chemie*	1,041	60	*Acta Chim. Acad. Sci. Hung.*	638
		104,410			30,607			16,343

cinal Chemistry have shown enormous growth—seven-fold and 4.5-fold, respectively.

Rapid communication journals have become very important. In 1960, the *Proceedings of the Chemical Society* contained 301 new compounds. By the time it changed its name to *Journal of the Chemical Society, Part D, Chemical Communications* in 1965, it contained 1,527 compounds a year, a five-fold increase, only to show a 3.6-fold increase by 1969 in which year it contained 5,415 compounds. In the same ten-year period, the yearly number of new compounds reported in *Tetrahedron Letters* increased from 876 to 6,272.

The output in the Soviet literature has grown considerably. Output for *Zhurnal Obshchei Khimii* grew steadily between 1960 and 1964, when it suddenly dropped off. This coincided with the publication of *Zhurnal Organicheskoi Khimii* and *Khimiya Geterotsiklicheskikh Soedinenii*. The combined output of these three journals increased by 100% during those years.

As shown in Table 3, analysis of journals by rank (in terms of yield of new compounds) shows that journals of rank 1 to 20 yield almost two-thirds of all compounds. Data are taken from the calendar year of 1969 but are also representative of other years.

Bradford's Law

According to Bradford's law[5] (illustrated in Fig. 1), one generally observes that a large part of the information in a specialized field can be obtained from a few top-ranking journals in that field. As the number of journals examined grows, the information gathered diminishes exponentially. In the case of synthetic chemistry, only seven journals were required to account for one-third of the compounds indexed in 1969. Only twenty-seven journals were required to cover two-thirds. More than 2,000 were needed to produce the last one-third. It is, however, more realistic to say that 158 journals account for the balance. In fact, 96% of the total output for 1969 was contained in only 100 journals. The dominance of a small key group of journals is much more dramatic in synthetic chemistry than that implied by a previous study[6], which reported that about 1,000 journals must be scanned to obtain 80% to 90% of the "chemical" literature reported in *Chemical Abstracts*. The *IC* census data correspond more closely to citation studies based on the *Science Citation Index* where it is found that the same small group of journals accounts for 90% or more of the citations appearing in chemical and other journals[7-9].

To support this finding to our own satisfaction, a separate study was conducted from 1967 to 1969 to make sure that no important chemical journals was overlooked. Article titles from 2,000 additional journals were searched by computer using ISI's Automatic Subject Citation Alert (ASCA). The project was discontinued when it became clear that these 2,000 journals only contributed 1% of the output obtained from less than 200 journals. As these journals were all covered in the *Science Citation Index*, the probability that pertinent information would be lost in a comprehensive literature search is very low indeed. Any cost-sensitive approach to information management must set some upper limit on the scope of any service[10].

Duplication for Searchers

The chief conclusions of our study are as follows. First, the synthetic chemical literature has been growing steadily at a rate of approximately 8.7% a year; second, English is increasingly the leading language of chemical communication and about two-thirds of the newly prepared compounds are re-

ported in English; third, one-third of all new chemical compounds are published in seven primary journals, half in fifteen, two-thirds in twenty-five; only 100 are needed to cover 96%.

As far as new synthetic chemistry is concerned, a cost effective service is provided by examining a carefully chosen
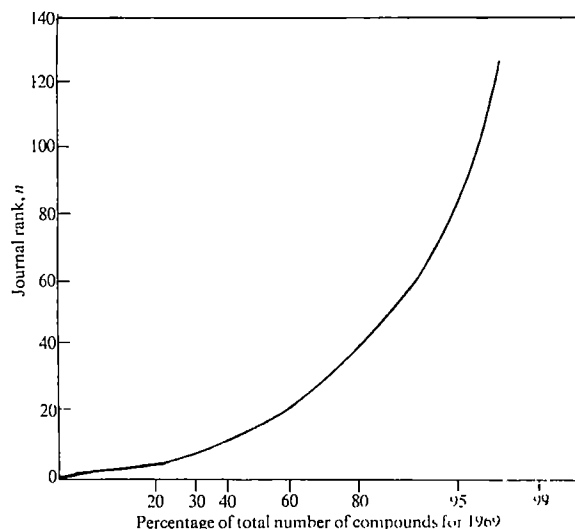
Fig. 1 Percentage of total number of compounds reported in 1969 for journals of rank $<n$. For $n=1$–20, the number of compounds is 104,361; for 21–40, 30,656; for 41–60, 16,343; for 61–80, 7,154; for 81–100, 5,238; for 101–183, 7,041.

and monitored list of 100 to 200 key journals. Although there may be other justifications for monitoring 12,000 journals at *Chemical Abstracts*[4], it certainly cannot be justified for the needs of synthetic chemistry.

Limitations

It may be argued that additional new compounds are found as a consequence of abstracting for other branches of chemistry, but there are economic limitations involved when one considers the exponential increase in computer and other costs involved if one must check all compounds, new and old, through a large-scale registry. Furthermore, the more intensive line by line examination and indexing of the more significant articles in synthetic chemistry, by contrast with indexing from abstracts, produces a number of not otherwise reported compounds, including thousands of intermediates.

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Five-Year Climatic Trend for the Northern Hemisphere

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Between May 1958 and April 1963 the mean temperature of the atmosphere in the northern hemisphere fell by about 0.60° C. The data which lead to this conclusion are presented in this article.

LARGELY as a result of possible man-made environmental effects, there attaches much interest at present to the study of observed climatic trends[1]. These trends may relate to regional conditions, or to the mean state of the entire atmosphere over one hemisphere or even over the whole Earth. Many studies of the latter two types have been made, usually from surface meteorological measurements[2-4]. These generally carry the lingering suspicion that perhaps the data used are too limited in space, chiefly vertically, to give a representative measure of conditions for, say, the air in the northern hemisphere as a whole. In order to improve this situation we have therefore computed, among certain other things, the mean temperature and water vapour content for the atmosphere in the northern hemisphere up to 75 mbar (about 18 km above sea level) by months from all available daily meteorological soundings during the five-year period which started on May 1, 1958. The mode of computing was such as to give the mass averages of the temperature and vapour content.

Treatment of Data

The data collection used comprises the so-called MIT General Circulation Data Library, which was compiled several years ago chiefly for the study of the dynamics of the atmosphere. It is the most refined and complete accumulation of daily meteorological data for the northern hemisphere, in convenient form for research purposes, now in existence. Its preparation,

checking and trial applications required a few years of labour. The total number of once a day (00Z) upper-air observing stations used was about 600 of which about 300 on the average reported useful measurements up to at least 500 mbar each day.

As the station network is irregular geographically, it was necessary to interpolate horizontally to secure values of the required quantities at regular gridpoints of a latitude–longitude net. This was done by objective computer analysis of the hemispheric data at each level according to a scheme devised by Oort and Rasmusson[5]. The temperature and humidity fields were thus analysed by months at the 1,000, 950, 900, 850, 700, 500, 400, 300, 200, 100 and 50 mbar levels. A few southern hemisphere equatorial stations were used in the analyses to help provide more accurate values in the tropics. From these analyses the vertical average temperature and specific humidity with respect to pressure were computed at each gridpoint for each month from the surface to the 75 mbar level. As the atmosphere is in close hydrostatic equilibrium, these vertical means constitute vertical mass averages.

The vertical averages were then integrated geographically, with proper mass weighting for each gridpoint, over the entire hemisphere or subregion of it. The hemispheric integration thus yielded sixty mass-average monthly values of the temperature and sixty more of the humidity for the atmosphere below the 75 mbar level. This upper limit implies that a little more than 92% of the atmosphere was included in the computations. Each monthly mean temperature is based on about 150,000 to 200,000 measured temperatures.

Our principal purpose here is to present the set of numbers which were obtained by the process outlined. It will thus be possible for those who so desire to analyse the material for the presence of a trend in such manner as they think proper, statistically or otherwise, or by combining it with other information to achieve other aims. As a simple example, however, we also present below our own trial analysis, possibly to serve as a basis for future discussion and to bring out certain further aspects of our data.

Table 1 Monthly Mean Hemispheric Mass-average Temperatures and Humidities for the Atmosphere between 0° N and 90° N

	1958–1959		1959–1960		1960–1961		1961–1962		1962–1963		Mean seasonal cycle	
	Temper-ature	Humidity	Temper-ature	Humidity	Temper-ature	Humidity	Temper-ature	Humidity	Temper-ature	Humidity	Temper-ature	Humidity
May	−15.58	3.05	−15.74	3.03	−15.79	3.07	−15.70	2.99	−16.33	3.02	−15.82	3.03
June	−13.54	3.53	−13.68	3.44	−13.69	3.46	−13.76	3.42	−14.21	3.34	−13.78	3.44
July	−12.31	3.83	−12.50	3.81	−12.54	3.84	−12.61	3.78	−12.94	3.71	−12.58	3.79
Aug.	−12.67	3.83	−12.64	3.83	−12.40	3.90	−12.79	3.82	−13.22	3.65	−12.74	3.80
Sept.	−14.24	3.51	−14.17	3.55	−14.33	3.54	−14.37	3.46	−14.62	3.44	−14.34	3.50
Oct.	−16.43	3.10	−16.47	3.06	−16.67	3.03	−16.83	3.02	−16.77	3.04	−16.63	3.05
Nov.	−18.66	2.71	−18.57	2.64	−18.86	2.63	−18.96	2.61	−18.96	2.65	−18.80	2.65
Dec.	−20.06	2.39	−20.00	2.37	−19.91	2.37	−20.51	2.31	−20.46	2.39	−20.19	2.37
Jan.	−20.49	2.19	−20.65	2.16	−20.72	2.16	−20.93	2.11	−21.13	2.19	−20.78	2.16
Feb.	−20.80	2.14	−20.50	2.18	−20.81	2.16	−20.71	2.13	−20.96	2.15	−20.76	2.15
March	−19.51	2.26	−20.18	2.32	−19.95	2.31	−20.09	2.33	−20.35	2.21	−20.02	2.28
April	−17.68	2.62	−18.12	2.65	−17.97	2.58	−18.30	2.55	−18.35	2.58	−18.08	2.59
Annual mean	−16.81	2.93	−16.94	2.92	−16.97	2.92	−17.13	2.88	−17.36	2.86	−17.04	2.90

The temperatures are in °C and the (specific) humidities are in g of water vapour kg⁻¹ moist air.

Monthly Means

Table 1 shows the sixty values of the hemispheric mean temperature. Table 1 also contains the corresponding sixty hemispheric mean specific humidity values. Table 2 lists sixty monthly mean temperatures and humidities similar to those in Table 1, but averaged over the complete zonal belt between the equator and 30° N. Table 3 gives similar mean temperatures and humidities but averaged over the remaining half of the hemisphere, that is from 30° N to the pole.

In our own sample analysis of the material the following procedure was used. It is clear that the data in Table 1 show a strong seasonal cyclic character. To investigate this property, a Fourier series of thirty terms was fitted to the sixty values. These are given in Table 4. As might be expected, the annual and semi-annual Fourier cycles have the largest amplitudes. The higher harmonics of the yearly variation, namely the 4, 3 and 2 month cycles, are smaller. As these five components could lead to a spurious trend for the five year period, they were in effect removed from the original numbers by subtracting the mean seasonal cycle. A graph of the temperature residuals is shown in Fig. 1a. As expected, all the seasonal cyclic components are absent, and the remaining variance is quite small. It is apparent by eye that the curve has a trend toward lower temperatures as the five-year period advances. To estimate this trend more objectively a linear trend line was fitted to the residuals by least-square methods (dashed line in Fig. 1a). It seems that there is a trend in the data toward decreasing temperature over the northern hemisphere of approximately 0.60° C (about 1.1° F) during the five-year period. The hemispheric humidity residuals computed in like fashion are depicted in Fig. 1d. They show a decrease of about 0.08 g of vapour kg^{-1} of (moist) air, again as computed from a linear trend line.

Figure 1b is analogous to Fig. 1a, save that it depicts the temperatures calculated for the belt between the equator and 30° N. The temperature trend in this case gives a cooling of about 0.81° C. Fig. 1c is again similar to Fig. 1a but shows the trend for the polar cap (30° N to 90° N). The cooling is 0.39° C. Fig. 1e shows the humidity residuals for the belt from 0° N to 30° N which give a linear decreasing trend of 0.10 g kg^{-1}. Finally, Fig. 1f gives the humidity residuals for the polar cap north of 30° N and shows a decreasing linear trend of 0.07 g kg^{-1} for the five years.

As an objective test of significance of the computed linear trends, we have computed 95% confidence intervals according to a method described by Kendall and Stuart[6]. Using their formula (28.93) we evaluated the confidence limits at the beginning (CI$_1$) and in the middle (CI$_{30}$) of the series. The resulting values are also shown in Fig. 1; they indicate the significance of the computed trends, at least as they apply during the five-year period.

The remaining three Figures show the contribution from different segments of the atmosphere to the integrated hemispheric trend. The first (Fig. 2) gives the five-year trend in the zonal mean temperature (that is, the temperature averaged with respect to longitude) for different levels and latitudes. We find strong cooling both in the subtropics and at very high latitudes. The cooling in the subtropics, however, dominates the hemispheric trend because it represents typical conditions over a larger area. There are some regions of computed heating, but they are of small magnitude and extent. They are chiefly located close to the Earth's surface, where the net hemispheric trend practically vanishes.

The contribution from different geographical regions to the hemispheric trend is shown in Fig. 3. In constructing this figure, the trend in vertical mean temperature was computed for each point of a 47 by 51 grid covering the hemisphere. The largest cooling rates are again found in the subtropics with

Table 2 Monthly Mean Mass-average Temperatures and Humidities for the Atmosphere between 0° N and 30° N

	1958–1959 Temperature	Humidity	1959–1960 Temperature	Humidity	1960–1961 Temperature	Humidity	1961–1962 Temperature	Humidity	1962–1963 Temperature	Humidity	Mean seasonal cycle Temperature	Humidity
May	−10.33	4.43	−10.82	4.37	−10.80	4.45	−10.91	4.31	−11.32	4.40	−10.84	4.39
June	−10.03	4.77	−10.27	4.59	−10.27	4.62	−10.74	4.54	−11.02	4.45	−10.46	4.59
July	−10.09	4.83	−10.55	4.75	−10.54	4.84	−10.78	4.73	−10.81	4.68	−10.55	4.76
Aug.	−10.27	4.87	−10.44	4.80	−10.03	4.98	−10.43	4.84	−10.96	4.65	−10.43	4.83
Sept.	−10.25	4.76	−10.36	4.81	−10.54	4.83	−10.75	4.68	−10.71	4.73	−10.52	4.76
Oct.	−10.86	4.51	−10.88	4.46	−11.11	4.45	−11.49	4.38	−11.30	4.43	−11.13	4.45
Nov.	−11.60	4.14	−11.57	4.01	−11.69	4.04	−12.19	3.95	−12.15	4.05	−11.84	4.04
Dec.	−12.23	3.71	−12.01	3.69	−12.19	3.73	−12.45	3.59	−12.66	3.75	−12.31	3.68
Jan.	−12.31	3.42	−12.41	3.37	−12.41	3.40	−12.46	3.29	−13.02	3.44	−12.52	3.38
Feb.	−12.46	3.37	−12.27	3.35	−12.69	3.38	−12.54	3.33	−13.17	3.41	−12.65	3.37
March	−11.80	3.49	−12.23	3.64	−12.21	3.62	−12.50	3.65	−12.68	3.47	−12.28	3.57
April	−11.34	3.94	−11.49	4.09	−11.68	3.91	−11.91	3.89	−11.93	3.93	−11.67	3.95
Annual mean	−11.13	4.19	−11.28	4.16	−11.35	4.19	−11.60	4.10	−11.81	4.12	−11.43	4.15

The temperatures are in °C and the (specific) humidities are in g of water vapour kg^{-1} moist air.

Table 3 Monthly Mean Mass-average Temperatures and Humidities for the Atmosphere between 30° N and 90° N

	1958–1959 Temperature	Humidity	1959–1960 Temperature	Humidity	1960–1961 Temperature	Humidity	1961–1962 Temperature	Humidity	1962–1963 Temperature	Humidity	Mean seasonal cycle Temperature	Humidity
May	−20.82	1.67	−20.66	1.70	−20.78	1.69	−20.49	1.68	−21.34	1.64	−20.82	1.69
June	−17.06	2.28	−17.10	2.29	−17.10	2.29	−16.77	2.30	−17.40	2.23	−17.08	2.28
July	−14.53	2.84	−14.45	2.87	−14.55	2.84	−14.43	2.83	−15.06	2.74	−14.60	2.82
Aug.	−15.07	2.79	−14.83	2.87	−14.77	2.83	−15.14	2.79	−15.47	2.66	−15.06	2.79
Sept.	−18.24	2.25	−17.98	2.29	−18.12	2.25	−18.00	2.24	−18.54	2.14	−18.16	2.23
Oct.	−22.00	1.69	−22.06	1.67	−22.22	1.60	−22.17	1.66	−22.24	1.65	−22.14	1.65
Nov.	−25.73	1.28	−25.57	1.27	−26.02	1.22	−25.73	1.27	−25.77	1.25	−25.76	1.26
Dec.	−27.89	1.07	−27.98	1.05	−27.62	1.00	−28.57	1.04	−28.26	1.02	−28.06	1.04
Jan.	−28.68	0.96	−28.89	0.95	−29.03	0.92	−29.40	0.92	−29.24	0.94	−29.05	0.94
Feb.	−29.15	0.91	−28.73	1.01	−28.93	0.94	−28.87	0.92	−28.75	0.90	−28.88	0.94
March	−27.22	1.03	−28.14	1.00	−27.68	1.01	−27.67	1.01	−28.02	0.95	−27.75	1.00
April	−24.01	1.29	−24.75	1.22	−24.25	1.26	−24.68	1.21	−24.78	1.23	−24.49	1.24
Annual mean	−22.53	1.67	−22.60	1.68	−22.59	1.65	−22.66	1.66	−22.91	1.61	−22.65	1.65

The temperatures are in °C and the (specific) humidities are in g of water vapour kg^{-1} moist air.
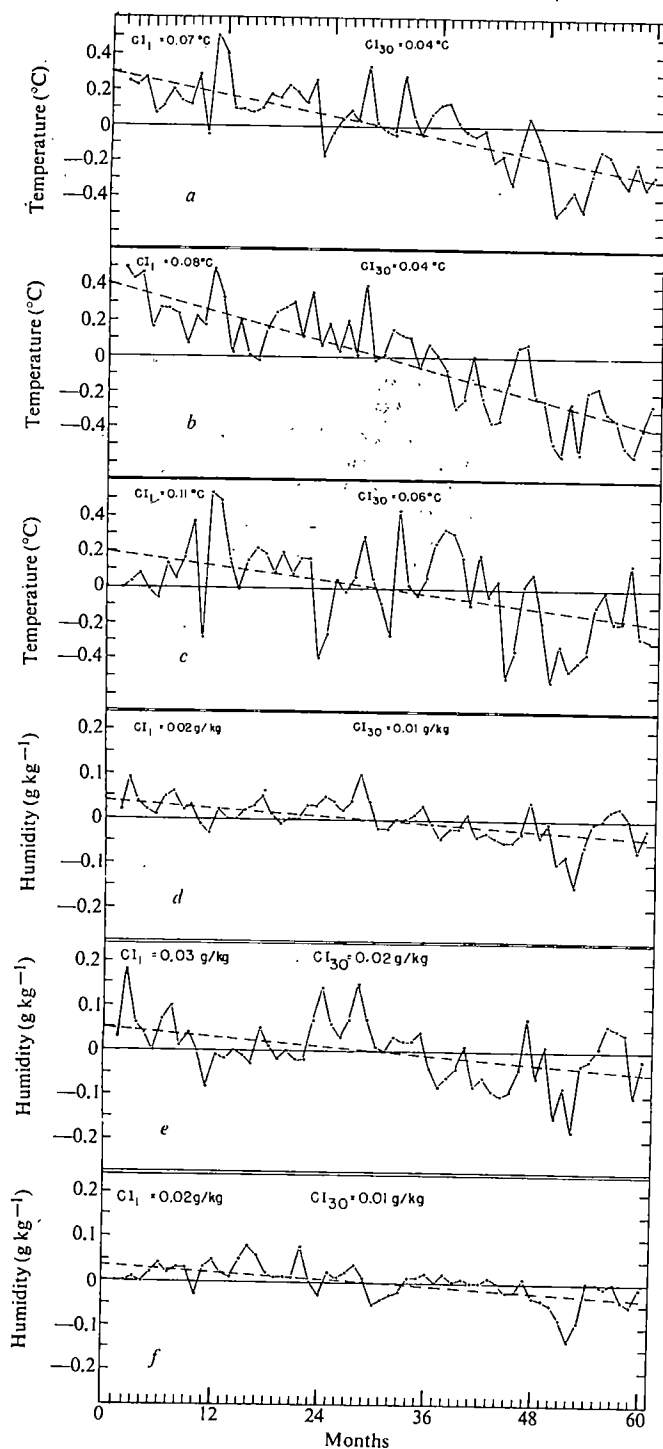
Fig. 1 Monthly mean mass-average values for the period May 1958 to April 1963. *a*, Hemispheric mean temperature; *b*, mean temperature 0° N to 30° N; *c*, mean temperature 30° N to 90° N; *d*, hemispheric mean specific humidity; *e*, mean specific humidity 0° N to 30° N; *f*, mean specific humidity 30° N to 90° N. - - -, Least-square linear trend lines. As described in the text the annual cycle was removed but otherwise the values are raw and unsmoothed.

Table 4 Results of Harmonic Analysis of Series of Monthly Temperature and Specific Humidity Averages over the Entire Northern Hemisphere for the Period May 1958 to April 1963

Period (months)	Temperature Amplitude (°C)	Temperature Phase (months)	Specific humidity Amplitude (10^{-3} g kg^{-1})	Specific humidity Phase (months)
60.0	0.21	17.5	34	16.4
30.0	0.12	6.3	19	1.1
20.0	0.02	2.5	14	2.6
15.0	0.03	2.2	5	−1.6
12.0	4.24	2.3	835	2.6
10.0	0.01	3.2	21	−4.8
8.6	0.10	1.8	9	3.5
7.5	0.05	1.5	16	1.7
6.7	0.04	−0.6	20	0.6
6.0	0.37	2.3	85	2.4
5.5	0.01	0.0	14	0.4
5.0	0.07	0.7	9	1.5
4.6	0.01	−1.6	5	0.9
4.3	0.04	1.6	5	1.2
4.0	0.08	−0.2	23	−1.2
3.8	0.04	0.8	14	0.7
3.5	0.05	−0.1	4	−0.5
3.3	0.05	0.6	2	−0.5
3.2	0.02	−1.5	6	−1.2
3.0	0.04	−0.6	8	−0.1
2.9	0.02	−1.0	4	−0.7
2.7	0.03	−0.5	2	−0.1
2.6	0.06	0.0	4	0.6
2.5	0.02	−0.0	4	1.0
2.4	0.01	−0.8	13	−0.3
2.3	0.01	1.1	7	−0.6
2.2	0.01	0.3	10	−1.0
2.1	0.04	−0.6	8	0.9
2.1	0.04	0.0	5	0.5
2.0	0.02	—	2	—

Phase is given as the time of nearest maximum in months following (or preceding) May 15, 1958.

the rest of the map. As a final item, the geographical distribution of the five-year trend in vertical mean humidity is shown in Fig. 4. The pattern is more complex than that of the temperature. In spite of the parallel downward trends in temperature and humidity on a hemispheric scale, the local trends are in some cases of opposite sign (see, for example, over Africa and India). In so far as these features are significant, the explanation of local differences should probably be in terms of an increase or decrease in adiabatic heating or cooling induced by dynamic processes.

Comments and Speculations

One of the first questions one may be inclined to ask is whether the downward trend in temperature and humidity can be extended beyond the five-year period. Past experience with other meteorological time series suggests that such a prediction would most likely lead to erroneous conclusions. Suppose, for example, that the calculated cooling in the northern hemisphere were to continue at the rate of −0.6° C every 5 yr for a century. Then the mean temperature would decrease by 12° C, a value which is clearly unrealistic. Thus, the downward trend in the 1958-1963 sample seems to represent part of a longer term natural fluctuation and probably will not continue in the decade following 1963.

This question clearly indicates the need to keep better track of the Earth's climate by reducing much longer representative data series than were used in the present study. It is indeed strange that—in spite of the extensive monitoring of local weather—one does not know the order of magnitude or even the sign of the changes which undoubtedly take place in the bulk of the atmosphere at the present time. Such knowledge is, of course, a prerequisite before one can assess the mechanisms responsible for climatic change and also the possible impact of man's activities on the climate. Both at the Massachusetts Institute of Technology and at the Geophysical Fluid Dynamics Laboratory of the National Oceanic and Atmospheric Administration projects are under way to extend the sample to after April 1963.

maxima over northern Africa and southern Asia. At this point it is relevant to mention the non-uniform character of the distribution of radiosonde stations over the Earth. Most stations are located over land and at middle latitudes. There are large gaps in the network south of about 20° N over the eastern North Pacific and the North Atlantic Ocean. Therefore one cannot fully discount the possibility of some compensating heating effect over part of the tropical oceans, which was overlooked in our analysis. Such a compensation seems unlikely, however, in view of the general cooling tendency over

Fig. 2 Latitude-height cross-section of the linear trend in the zonal mean temperature during the period May 1958 to April 1963 (°C/5 yr).
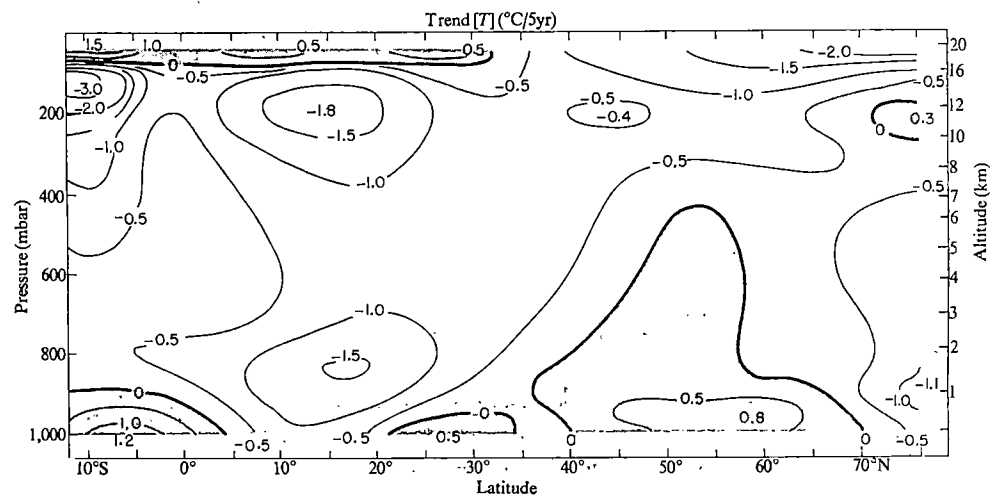
Up to this point we have discussed the situation in the northern hemisphere. In the southern hemisphere, the distribution of upper air stations is quite poor by comparison. Recent developments in measuring vertical temperature profiles from meteorological satellites promise, however, an improvement in the future monitoring of the climate over the entire Earth.

Aside from registering slow changes in the heat content of the atmosphere, it will be important to expand and coordinate efforts to measure changes in heat storage in the other components of the Earth–atmosphere system. For example, the water in the oceans and also the snow and ice in glaciers and in the ice caps can either store or release huge amounts of heat and thereby affect the Earth's climate. In this connexion, it may be of interest to note that since about 1958 there seems to have been a rather uniform trend toward lower values of the surface temperature both in the North Atlantic Ocean[7,8] and in the North Pacific Ocean[9].

As to an explanation of the cause or causes of climatic trends such as those presented here, the field is wide open for speculation. First of all, there are astronomical factors involved such as the solar constant, its annual variation and the spectral

Fig. 4 Geographical distribution of the linear trend in the vertical mean (mass-weighted) specific humidity during the period May 1958 to April 1963 (g kg^{-1}/5 yr).

distribution of the incoming solar radiation. In addition, there is the possibility of internally generated cycles caused by factors in the atmosphere–ocean–cryosphere system itself. For instance, changes in chemical composition of the atmosphere, changes in albedo of the solid Earth arising from variations in vegetation, snow or ice cover, and changes in temperature of the ocean surface would strongly affect the atmospheric heat balance.

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Fig. 3 Geographical distribution of the linear trend in the vertical mean (mass-weighted) temperature during the period May 1958 to April 1963 (°C/5 yr).

Reactions between an Insect Picornavirus and Naturally Occurring IgM Antibodies in Several Mammalian Species

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Domestic and wild animals have IgM antibodies which react with insect viruses. Infection by agents sharing common antigens with the insect viruses could account for this phenomenon.

THE use of viruses to control insect pests is attractive because of the undoubted economic advantage and apparent high degree of specificity. Insect viruses are claimed to have a restricted host range and there are no records of transmission to animals outside the class Insecta. Here, however, we describe serological reactions between a picornavirus which infects *Gonometa podocarpi* (Lepidoptera: Lasiocampidae) and naturally occurring antibodies in several mammalian species, which suggests that the animals may have been exposed to the virus or a serologically related antigen.

Serological Relationships

Gonometa virus is morphologically similar to the small RNA viruses infecting vertebrates and also resembles them in several physico-chemical properties; for example, it contains 37% single-stranded RNA, the protein moiety comprises four polypeptides with molecular weights ranging from 36,500 to 12,000 and the virus has a buoyant density of 1.35 g cm³ in caesium chloride[1]. Tests were therefore made to determine whether any serological relationships existed between the *Gonometa* virus and vertebrate picornaviruses. Bovine enterovirus VG-5-27[2], porcine enterovirus Italian 1/66[3], encephalomyocarditis virus, vesicular exanthema virus and several serotypes of foot-and-mouth disease virus, each of which gave a precipitation line with its homologous antiserum in immunodiffusion tests, did not react with *Gonometa* virus antisera which had been produced in rabbits and guinea-pigs and gave a homologous reaction at a dilution of 1/16. Nor were precipitation lines obtained between the *Gonometa* virus and hyperimmune guinea-pig antisera to the vertebrate viruses listed above.

The chance observation, however, that sera from pigs infected with the Italian 1/66 virus produced a precipitation line with purified *Gonometa* virus prompted a more detailed examination of this reaction. When sera from pigs infected with foot-and-mouth disease were reacted with purified *Gonometa* virus, a precipitation line appeared in each test. This line gave a pattern of non-identity with the line produced

by the same serum and foot-and-mouth disease virus particles but it did fuse with that produced by *Gonometa* virus and its homologous rabbit antiserum (Fig. 1). Moreover, pre-inoculation sera from all the animals subsequently infected with foot-and-mouth disease virus also gave a precipitation line with *Gonometa* virus and all the six sera we examined were strongly positive.

IgM Antibody

The substance in the pig serum giving this reaction was stable at 56° C, but precipitating activity was destroyed when the serum was treated overnight with 0.1 M 2-mercaptoethanol. This suggested that the reaction involved IgM antibody and the following confirmatory evidence has been obtained.

Serum from a pig infected 7 days previously with foot-and-mouth disease virus was centrifuged for 16 h at 90,000g in a 15–25% sucrose gradient. Fractions from the gradient were concentrated with half-saturated ammonium sulphate and tested with *Gonometa* virus and foot-and-mouth disease virus. The fractions from the 19S region of the gradient gave a precipitation line with each virus (Fig. 2). Serum from an animal infected some weeks previously was fractionated similarly. The fractions from the 19S region of the gradient with this serum gave a line with *Gonometa* virus and a weak reaction with foot-and-mouth disease virus, whereas the fractions from the 7S region gave a reaction with foot-and-mouth disease virus only.

Serum samples from a pig infected with foot-and-mouth disease virus were electrophoresed in agarose and the separated
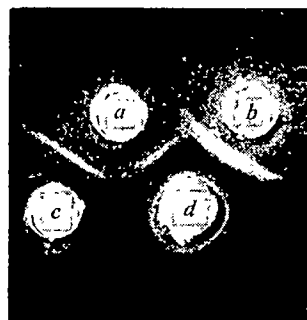
Fig. 1 Immunodiffusion test with *Gonometa* virus (*a*), foot-and-mouth disease virus (*b*), rabbit antiserum to *Gonometa* virus (*c*) and serum from a pig infected with foot-and-mouth disease virus (*d*). The test shows the identity of the lines produced with *Gonometa* virus and the two sera and the non-identity of the lines produced with the pig serum and the two viruses.

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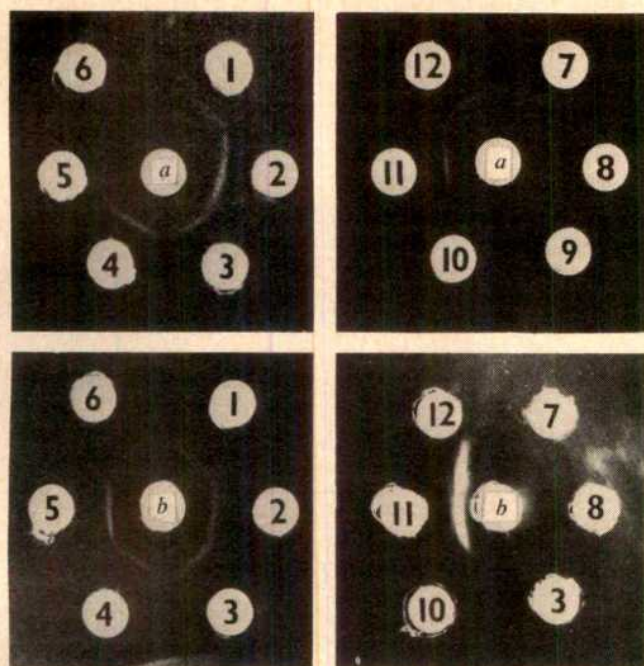
Fig. 2 Immunodiffusion test of the fractions prepared by sucrose gradient centrifugation of pig serum obtained seven days after infection with foot-and-mouth disease virus, using *Gonometa* virus (*a*) and the homologous foot-and-mouth disease virus (*b*) as antigens. 1–10 refer to the sucrose gradient fractions, numbered from the bottom of the tube. Unfractionated pig serum and rabbit antiserum to *Gonometa* virus are at positions 11 and 12.

proteins then allowed to diffuse towards channels containing *Gonometa* virus or foot-and-mouth disease virus. Serum taken 7 days post-infection gave a precipitation line with each

virus at the position of IgM. Serum collected 18 days post-infection gave a line with *Gonometa* virus only at the IgM position, whereas the reaction with foot-and-mouth disease virus was mainly at the position of IgG.

Mixtures of *Gonometa* virus and purified IgM antibody from pig serum were examined in the electron microscope. Complexes were observed which were similar to those obtained with foot-and-mouth disease virus and the homologous IgM antibody[4] and with *Gonometa* virus and its homologous IgM antibody. The complexes of *Gonometa* virus and IgM antibody from pig serum showed attachment of antibody molecules at regular intervals on the virus surface (Fig. 3). In contrast, complexes of *Gonometa* virus with the homologous IgG antibody showed attachment of the antibody molecules over the entire surface of the virus.

The *Gonometa* virus did not react with the IgG fraction prepared by DEAE-cellulose chromatography of serum from pigs infected with foot-and-mouth disease virus. This IgG antibody preparation gave a precipitation line with the homologous virus.

In all the tests described, the *Gonometa* virus particles had been purified by sucrose gradient and caesium chloride centrifugation. The supernatant from the infected insect homogenate, from which the virus had been pelleted at 80,000*g*, did not give a reaction with the pig serum. This indicated that soluble insect proteins did not react non-specifically with any components of the pig serum. Further, a recently isolated virus from *Darna trima* (Lepidoptera: Limacodidae) (J. S. R. and J. F. L., unpublished data), obtained from Sabah (formerly Borneo), which is not related serologically to the *Gonometa* virus, also gave a precipitation line with the pig serum and this did not fuse with the line produced by *Gonometa* virus (Fig. 4); thus, these reactions are not identical. These observations suggest that the reaction between *Gonometa* virus and pig serum is specific.

Because natural antibodies of the IgM class are found in the sera of a wide range of animals, pig serum giving a strong
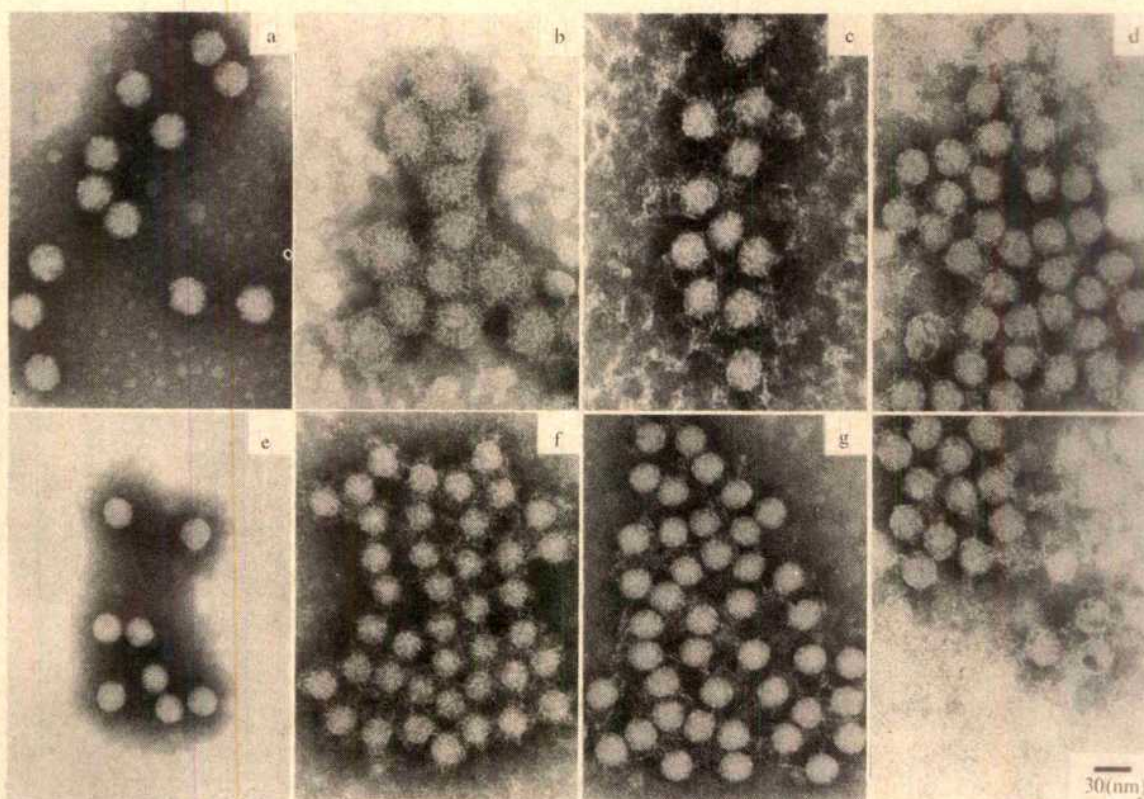
Fig. 3 Electron micrographs of complexes of *Gonometa* virus with the specific IgG and IgM antibodies and with the IgM fraction of pig serum compared with those obtained with foot-and-mouth disease virus and the specific IgG and IgM antibodies: *a*, *Gonometa* virus alone; *b*, plus IgG; *c*, plus IgM; *d*, plus IgM fraction from pig serum; *e*, FMDV alone; *f*, plus IgG; *g*, plus IgM.

Fig. 4 Immunodiffusion test of *Gonometa* virus (*a*) and *Darna trima* virus (*b*) with pig serum (*c*), showing the lack of identity in the two reactions.

reaction with *Gonometa* virus was tested with a range of bacterial antigens which have been shown to react in some cases with IgM from animals not experimentally exposed to the antigens. Only one of ten antigens, namely *Salmonella minnesota* glycolipid, gave a precipitation reaction with the pig serum and this line did not fuse with that produced by *Gonometa* virus. Furthermore, as antigens on sheep red blood cells react with sera from other species, pig serum which had been absorbed with sheep red blood cells was tested with *Gonometa* and *Darna trima* viruses. The absorbed serum gave a precipitation line with each virus.

Reactions with Other Species

The sera of several other species have also been tested for their reactivity with *Gonometa* virus. Reactions were obtained with sera from cattle (10/10), sheep (4/6), horses (4/6), dogs (1/6) and three species of deer (10/10). The intensity of the reaction varied considerably in individual animals of the same species, for example, some undiluted sera gave only a faint reaction whereas reactions were occasionally obtained with sera diluted 1/8. The precipitation lines obtained with the different species fused, providing further evidence for the specificity of the reaction. No reactions were obtained with sera from guinea-pigs and rabbits which had been reared for laboratory purposes, nor with wild rabbit sera. It was significant that sera obtained from gnotobiotic pigs (6 animals) and cattle (6 animals) did not react with *Gonometa* virus.

These observations raise some important questions, particularly as to the stimulus which produces IgM antibody in these animal species. It is possible that the reaction occurred because the animals had previously been exposed to *Gonometa* virus. As the *Gonometa* virus was isolated from an insect species which is indigenous to East Africa and has not been recorded elsewhere, it seems unlikely that this virus induced the response. The class Insecta contains some 75% of the known animal species, however, of which only a small number have been examined for the viruses they may harbour, and it is quite feasible that the *Gonometa* virus or serologically related viruses occur in other parts of the world. Indeed, in some instances, close serological relationships have been demonstrated between viruses isolated from quite unrelated insects whose habitats are widely separated geographically[5,6]. It is possible therefore that there are viruses either of invertebrate or of vertebrate origin which are widely prevalent in the United Kingdom which share common antigens with the *Gonometa* virus.

It is not clear why the response involves only IgM antibodies but this could be explained on the basis of a low but frequently repeated stimulus. There are several reports in the literature of the presence of virus-neutralizing substances in the sera of animal species not regarded as natural hosts. Cattle sera from Sierra Leone, Ghana, Uganda, Sudan and Kenya contained neutralizing substances, probably antibodies, against yellow fever virus[7]. This was also true, however, of 3/40 cattle sera

from India and 1/153 from England and France, where exposure to infection with yellow fever virus could be ruled out. The phenomenon of neutralizing substances to polio virus in cows has been reviewed[8]; serum from 75–90% of cattle over three years of age neutralized not only type 2 polio virus but also type 1 and occasionally type 3. The neutralizing substances were usually present in low titre but possessed all the properties of antibody in human sera, including a predominant association with the gamma globulin fraction. In calves of four to six months of age, neutralizing substances were rarely found. A significant feature of this work was that calves without neutralizing antibody could not be infected with a virulent strain of polio virus, irrespective of portal of entry, and moreover failed to develop antibodies to it. Sabin[8] concluded that "in cattle, at least, the antibody appearing in low titre with advancing age was probably the result of infection with another agent possessing antigenic groups that are related to those of poliomyelitis virus". A more recent observation is the presence in pigs in Japan of high levels of neutralizing antibody to *Nodamura* virus[9], which has been tentatively classified as a picornavirus[10]. Neutralizing antibody was also found in 1/54 herons and egrets[9], and it was concluded that pigs were the likely source of *Nodamura* virus, since they were frequently bitten by *Culex tritaeniorhyncus*, the mosquito from which the virus was first isolated. The nature of the neutralizing antibodies has not been determined, so it is not known if IgG or IgM is involved.

These observations with *Gonometa* and *Darna trima* viruses have implications relating to the control of insect pest populations by the deliberate release of viruses. While it is probably true that most insect viruses exhibit a high degree of host specificity and thus have great potential in biological control programmes, it is obviously desirable that sound experimental data should be available to check this specificity. It seems unlikely that the antibody to the two insect viruses resulted from infection and multiplication of similar agents in the mammalian hosts. The IgM response implies repeated low level exposure to the antigen concerned which must therefore be widely distributed in the environment. The close relationship of these antigens to the two viruses suggests the existence of viruses in some host population, possibly arthropod, in the areas from which our serum samples were drawn. The ubiquity of these agents and the apparent regularity with which they can reach mammalian hosts stress the risks which might arise from the deliberate release of virus to control insect pest populations, should the viruses used exhibit wider host specificity than expected.

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LETTERS TO NATURE

PHYSICAL SCIENCES

Another Test of Space-Time Curvature and Relativity

Now * that Sir Arthur Eddington has successfully measured the space-time curvature by the edge of the Sun, thereby confirming Dr Einstein's remarkable forecast, an additional test of relativity comes to mind.

Obviously space must be curved through a physical fourth dimension. The fact that we cannot actually see the curvature should not cloud our perception of it. Minkowski by his interpretation of $\sqrt{-1}$ provides a precise mathematical demonstration of the curvature of space to form the hypersurface of a hypersphere. Therefore light coming to us from distant sources must necessarily have traced out this space-time curvature. In other words, it must have been on the average in a constant state of acceleration throughout the journey from its source.

When Heinrich Olber propounded his paradox in 1826 almost one hundred years ago, he assumed that the intrinsic brightness of starlight would remain unchanged, regardless of the distance traversed. He, of course, took it for granted that space was Newtonian space—"flat". With relativity this premise is altered. Space is curved through a fourth dimension; light following the curvature must be accelerating; and consequently the intrinsic brightness of starlight must be reduced to an apparent brightness in direct proportion on the average to the distance covered. Olber's paradox is thereby resolved.

Also, another test of relativity and space-time curvature is provided. By looking further and further out into space astronomers should be able to detect a red shift in starlight—a shift that increases in direct proportion to the distance covered. Perhaps when Dr Hubble gets his 100-inch telescope into operation the test will become feasible.

It is important, I believe, that astronomers should be informed now that the red shift is to be expected. Otherwise, when they find it, they may adopt a three-dimensional interpretation. If so, on the basis of a Doppler effect they could reach an erroneous conclusion that the universe was exploding. Nor can we count on the more conservative and orthodox physicists of today to correct the error. Being predominantly three-dimensional minded they might easily fall in with the same false reasoning. Such a calamity could set relativistic physics back by half a century.

In order to prevent this from happening it may be just as well to scotch such an interpretation at the outset. The correct interpretation is readily obtained by considering a three-dimensional analogy. Suppose a spherical balloon is covered with polka dots. From a two-dimensional viewpoint at the surface of the balloon light coming from distant polka dots would be coming around a curve. This three-dimensional curvature would be beyond the two-dimensional viewpoint. Yet the red shift in the light would be observable. It would be a shift that increased on the average in direct proportion to distance.

Now suppose the balloon was in the process of being blown

* Copy of a manuscript found in the drawer of a desk built in 1922. Communicated by H. W. Grayson.

up to larger size. The polka dots would be spreading apart, thereby creating a Doppler-type red shift. At the same time, over a given distance, the rate of curvature into the third dimension would be decreasing, thereby decreasing the rate of acceleration and reducing the three-dimensional red shift. The two changes in the red shift would exactly offset each other, so that from the two-dimensional viewpoint at the surface of the balloon there would be no evidence that the balloon was expanding. The same in reverse would be true if the balloon was shrinking.

We in three-dimensional space which forms the hypersurface of a hypersphere are in a similar situation. There is no way we can observe whether our universe is expanding, contracting or stable. There is, of course, the question whether or not Dr Einstein's field equations provide for a stable universe. Yet that is a theoretical problem still moot. It would be unfortunate if the red shift, when it is discovered, should serve to obfuscate a solution to Dr Einstein's problem.

The important point is that by looking far enough out into space, astronomers should be able to detect a red shift in starlight. Moreover, this red shift when it is discovered will provide additional confirmation of Einsteinian space-time curvature and relativity.

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The Origin of the Moon

I HAVE some quantitative doubts concerning Anderson's proposals[1] that the Moon condensed from material off the median plane of the initial solar nebula.

First, the pressure range which he uses for his solar nebula seems to be rather high, and, of course, the partial pressures of the components will be well below the total. But a temperature adjustment could compensate for that. Much more serious is the fact that when condensation begins in the lower pressure region away from the median plane, the resulting dust particles will fall slowly through the residual gas towards this plane. The "scale height" for a dust particle with only 100 atoms in it will be 10 times less than that for one atom (in the absence of condensations the gravitational potential energy increases as the square of the distance from the median plane). Any heavier particles will necessarily and quickly congregate very close to the median plane, when they will be swept up by the developing Earth.

If the gas were dense, convective movements would no doubt modify extensively the distribution of both gas and dust, but would quite certainly not allow particles initially condensing off the median plane to remain there until they had formed the Moon.

If the bulk of the Moon is systematically more refractory than that of the Earth it seems to me inescapably to follow that it must originally have formed nearer the Sun.

All existing explanations of the Moon's origin are improbable—and perhaps need to be in view of the unique character of the Earth–Moon system—but if it had formed within the orbit of Mercury, a resonant interaction with the

latter might have led to its ejection, leaving Mercury in a highly eccentric orbit which has even yet not become so nearly circular as the orbits of Venus or Earth[2].

Although I do not believe Anderson's theory of the formation of the Moon, his idea of differential volatility may be important.

To me, it seems easier to believe that the material of the planets was collected by the Sun in passing through a cold dust cloud rather than from the remains of the solar nebula. A dust cloud would have an angular momentum, resulting from its motion around the centre of the Galaxy, of the right order of magnitude for our planetary system —whatever redistribution between it and the Sun might later occur—and the evaporation of the more volatile particles as they approached the Sun from all sides would build up an adequate capture mechanism both for each other and for more refractory particles.

Whether or not this was so, if the actual accumulation into planets took place with the Sun close to its present temperature, it is important that water, surely the most abundant compound of oxygen and hence perhaps of all elements, would be in the form of dust further away from the Sun than the asteroids but in the form of gas within this region.

Clearly gases could not have contributed to the primary aggregation leading to the inner planets, which would have been within the Roche limit for any reasonable gas pressure.

It seems uneconomical to have a different mechanism for the accumulation of the outer planets, and the properties of water give us the opportunity to use the same mechanism and still explain their very different structure. The presence of ice crystals in quantity will have led to a discontinuous rise by a large factor in available material beyond the asteroid belt, leading to a faster and earlier beginning for the major planets. These would then have reached a mass which could capture first methane and then hydrogen well before the inner planets could do so and hence, as observed, have swept up almost the whole of the system's supply before the Earth and Venus were big enough to take their share.

I am not confidently supporting Ovenden's[3] proposal for a planet 90 times the mass of the Earth in the region of the asteroids, because I do not see how one can be sure that small cumulative errors do not invalidate his calculations. Nevertheless, if this had been formed chiefly of water and hydrogen, and its destruction had been due to its orbit coming into resonance with Jupiter and its consequent deflexion to an approach within the Roche limit, there would be no problem of accounting for what had happened to 99.9% of its mass. Jupiter will have it, but a belt of gas might have persisted for long enough to bring the residual solid particles back to their present orbits.

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Bode's Law

M. W. OVENDEN[1] has outlined a theory intended to provide a dynamical explanation for Bode's Law. I suggest instead that the approximately constant spacing ratio expressed in Bode's mnemonic can be generated by a sequence of random numbers subject to the constraint that adjacent planets cannot be "too close to each other". The physical basis for the constraint is that if in the process of accretion two planets were "too close
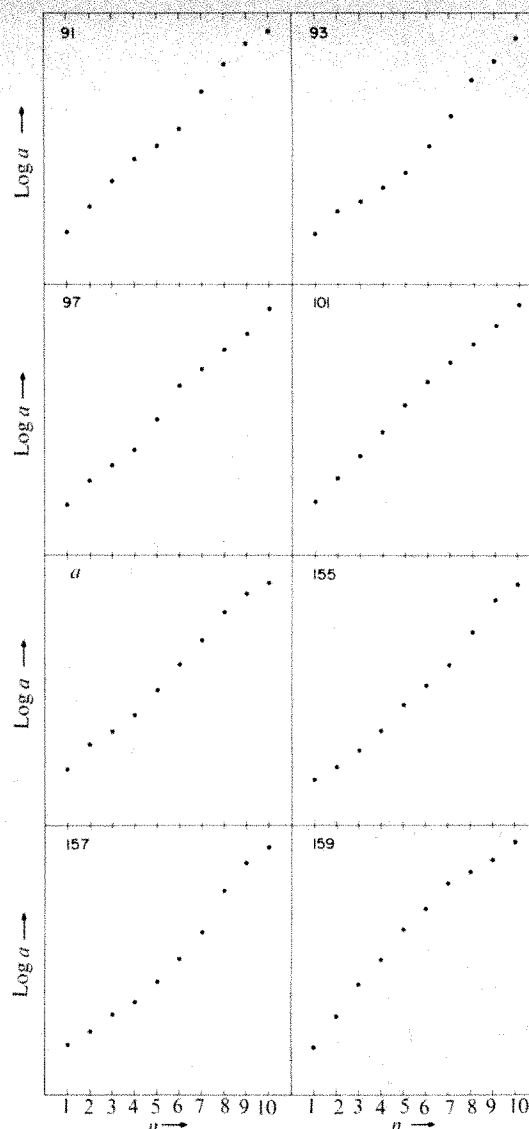
Fig. 1 Bode's Law for computer-simulated planetary systems.

to each other", they would coalesce or cease to grow because they were competing for the same material. Such a constraint was embodied in a series of computer-generated planetary systems published by S. H. Dole[2]. Dole generated planets by injecting nuclei into a Laplace-type nebula and allowing them to accrete dust and also gas (if their mass was sufficiently large and their temperature sufficiently low). He kept track of the dust and gas accreted (so that it could not be used twice) and coalesced planets if their orbits crossed. The initial semimajor axes of the proto-planets were chosen at random.

In Fig. 1 is plotted the logarithm of the semimajor axes (a_n) against the planet number (n) for seven of Dole's computer-generated planetary systems and for the Solar System. The reader is invited to pick out the Solar System. (The label for the Solar System in binary is 111001. The remaining labels are Dole's.)

The slopes $(\log (a_9) - \log(a_2))/(9-2)$ cover a narrow range bracketed by the slopes of the lines in Fig. 2. The fractions to the right of each line give the ratio of adjacent planetary periods corresponding to the plotted ratio of semimajor axes. It is seen that within this narrow range the ratio of periods is always close to that of two "small" integers.

I conclude that this offers an equally satisfactory rationalization of Bode's mnemonic. Further, I suggest that the closer spacing of the satellite system compared with the spacing of planets in the Solar System might be accounted for by the fact that the satellites did not grow to a size where they accreted gas (in addition to dust) and that their accretion was not
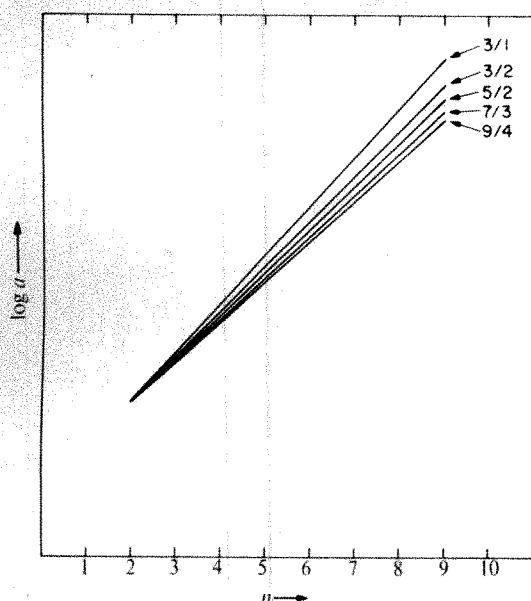
Fig. 2 Slopes for which ratio of adjacent periods is rational.

appreciably helped by their self-gravity. Thus they consumed a smaller fraction of their surrounding nebula and could be formed closer together. A computer simulation of satellite systems, following Dole's model, would provide evidence with which to evaluate this speculation.

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Underabundance of Ionized Helium in the Galactic Centre

GAMOW[1] suggested in a classical paper that the present element abundances (in particular the light elements H, D, He and Li) may have been formed during the first few minutes of the birth of the universe. This suggestion received further support after the 3 K background radiation, also implied in that paper and numerically predicted by Alpher and Herman[2], was

detected by Penzias and Wilson[3]. There are, however, still serious objections to a primordial origin for helium.

The most direct method of determining helium abundances in our Galaxy with the least number of complicating assumptions is the observation of hydrogen and helium radio recombination lines in HII regions. The basic method, its assumptions, and its uncertainties are discussed in, for example, refs. 4, 5. If we assume that hydrogen and helium are homogeneously mixed and that hydrogen is ionized wherever helium is ionized, then the total helium abundance is given by

$$\frac{N_{He}}{N_H} = \frac{N_{He}^\circ}{N_H^+} + \frac{N_{He}^+}{N_H^+} + \frac{N_{He}^{2+}}{N_H^+}$$

The second and third terms on the right can be determined by observation of radio recombination lines.

Most cosmological models predict a helium abundance of approximately 10% by number. In an effort to determine whether this value holds throughout our Galaxy we have observed hydrogen and helium radio recombination lines in 40 galactic HII regions. These data will be published in detail later (Churchwell, Mezger and Huchtmeier). A brief summary of the primary results is as follows:

There are HII regions, such as NGC 2024 and M43, with a very low N_{He}^+/N_H^+ ratio. These are HII regions whose exciting stars are of spectral type 09 or later. Theoretical considerations[6] show that stars with such low effective temperatures cannot ionize a substantial amount of helium.

All HII regions located at galactic radii $R \gtrsim 3$ kpc which require for their ionization one (several) star(s) of spectral type 07 or earlier have abundances in the range

$$5\% \le N_{He+}/N_H^+ \le 12\%$$

with most values clustering around 9%. This result supports the conclusion drawn from an analysis of various observational methods that the He-abundance at least within our Galaxy is constant and has a value (number ratio) of about 10% (ref. 7).

In agreement with estimates of the effective temperatures of early-type stars, the amount of doubly ionized helium, He²⁺, in galactic HII regions is negligible.

Only in the case of three giant HII regions (the definition of a giant HII region is that its intrinsic radio flux density for $\tau_c \ll 1$ is equal to or greater than four times the flux density of the Orion Nebula) with projected positions close to the galactic centre was it not possible to detect helium lines[8,9]. We have investigated the distribution, distance and kinematics of the ionized hydrogen towards the galactic centre region, and conclude that giant HII regions located within $-1° \le l^{II} \le +1°$ and close to the galactic plane have actual distances of less than 150 pc from the dynamical centre of the galaxy[10].

The possibility that the helium might be in the doubly ionized state prompted us to search for the He⁺173α line in

Table 1 Observed Helium Abundances

Source	HPBW (arc min)	Integ. time (min)	Transition	T_L (K)	$\frac{\varepsilon(137\beta)}{\varepsilon(109\alpha)}$	$\varepsilon = \int T_L dv$ (K kHz)	$\frac{N(He^+)}{N(H^+)}$	$\frac{N(He^{2+})}{N(H^+)}$	Ref.
G0.2–0.0	6	510	H109α	0.247 ± 0.006	—	200 ± 17			
	6	510	He109α	≤ 0.006		≤ 5	≤ 0.025		
	6	666	He⁺173α	≤ 0.008		≤ 6		≤ 0.008	
G0.5–0.0	4	105	H109α	—	—	—			11
	4	105	He109α	—		—	≤ 0.041		11
G0.7–0.0	6	450	H109α	0.245 ± 0.005		141 ± 16			
	6	450	He109α	≤ 0.005	0.257 ± 0.035	≤ 3	≤ 0.021		
	6	494	He⁺173α	≤ 0.005		≤ 3		≤ 0.005	
	4	75	H109α	—	—	—			11
	4	75	He109α	—		—	≤ 0.039		11

For sources G0.2–0.0 and G0.7–0.0 only data for the main line components are reported.
To obtain N(He⁺)/N(H⁺) we assumed that $\Delta v_L(He) = \Delta v_L(H)$ where Δv_L is the line width at the half-intensity point.
Neither T_L nor ε values are given by ref. 11.

Fig. 1 109α recombination spectrum of G0.7–0.0. ——, Best fit to the observed data points; - - -, the two gaussian components of the H109α line, determined by a best fit decomposition. Inset: the expected He109α profile which was obtained by scaling the H109α profile by a factor of 0.1 and shifting it by +2.041 MHz with respect to the centre frequencies of the two H109α components. A C109α line may be present with a velocity of ~ +50 km s^{-1} to the high frequency side of where the helium lines are expected.
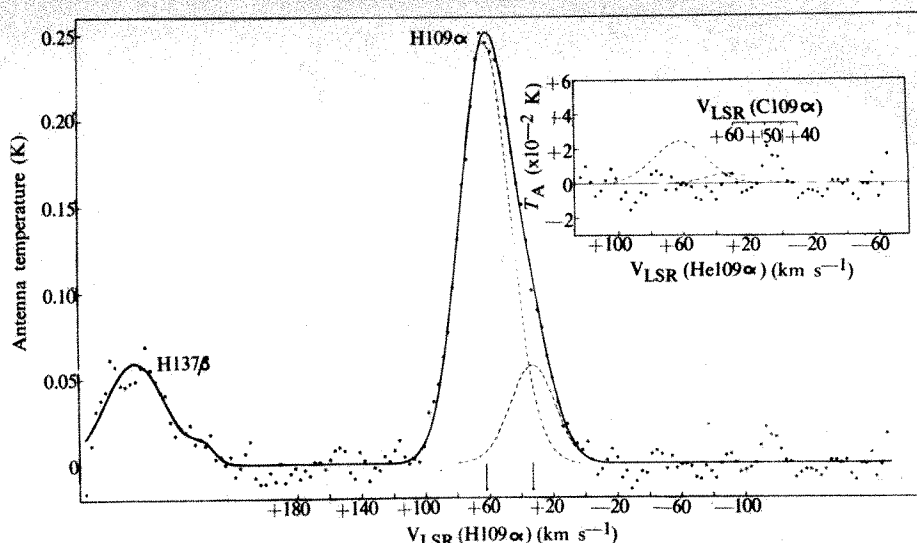
G0.7–0.0 and G0.2–0.0, with negative results. Recently, Huchtmeier and Batchelor, using the Parkes 210-foot telescope, have found an upper limit on the He$^+$ abundance in G0.5–0.0 considerably lower than the values given in Table 1.

Our observational results, obtained with the NRAO 140-foot telescope in conjunction with a 384 channel auto-correlation spectrometer, are compiled in Table 1. Also included are some earlier measurements[11] with the Parkes 210-foot telescope.

G0.5–0.0 has a gaussian hydrogen line shape, whereas G0.2–0.0 and G0.7–0.0 have more complex hydrogen line shapes which can be interpreted as a superposition of several velocity components. Fig. 1 shows as an example the 109α recombination spectrum of G0.7–0.0.

The two gaussian components (best-fit) are indicated by dashed curves. The inset in Fig. 1 shows the expected He109α profile.

The abundance of He$^+$ in all these HII regions is less than 2%. (We include G0.5–0.0 on the basis of the Huchtmeier and Batchelor results.) The abundance of He^{2+} in G0.2–0.0 and G0.7–0.0 is less than 1%. Either the helium is essentially all neutral or there is no helium in the galactic centre. We will briefly discuss these two possibilities.

It has been shown that these nebulae are similar to giant spiral arm HII regions such as W49A (ref. 10). The number of 09-stars that would be required to ionize these HII regions makes ionization by such cool stars unlikely, unless the luminosity function of 0-stars in the centre region is drastically different from that in the solar vicinity. This, together with the results of Rubin[6], makes it rather unlikely that a large fraction of helium in these HII regions exists in the neutral state. This would imply that there is an actual underabundance of helium in the galactic centre.

The cosmological implication of a helium underabundance in the galactic centre would be far reaching. We do not overlook that there are also a number of giant spiral arm HII regions with an abundance of He$^+$ considerably less than 10%. On the other hand, in no giant spiral arm HII region do we observe an abundance of He$^+$ as low as 2%. Our observations of the galactic centre region, however, show that $N(He^+)/N(H^+)$ and $N(He^{2+})/N(H^+)$ are respectively <2% and <1%. Therefore, 70% of the total helium content in the galactic centre HII regions would have to be neutral if the He abundance were the same as in the spiral arms. The NRAO is operated by Associated Universities, Inc., under contract with the National Science Foundation.

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Table 2 Characteristics of HII Regions

Source	Size θ_α (pc)	θ_δ (pc)	D kpc	$S_{5\ GHz}$ f.u.	L_c s^{-1}	No. of stars required 07	09
G0.2–0.0	51	15	10	157	1.65×10^{51}	97	424
G0.5–0.0	13	16	10	35.5	3.04×10^{50}	18	78
G0.7–0.0	9	11	10	47.8	4.63×10^{50}	27	119

Some characteristics of the HII regions, derived from continuum observations at radio wavelengths, are compiled in Table 2. The data for the source size (columns 2 and 3) and flux density at 5 GHz (column 5) were taken from Reifenstein *et al.*[12]. The Lyman continuum photon flux required to produce the measured radio flux density (column 6) was derived using the relation (valid for $\tau_c \ll 1$)

$$\left[\frac{L_c}{s^{-1}} \right] = 4.76 \times 10^{48} \left[\frac{\nu}{GHz} \right]^{0.1} \left[\frac{T_e}{K} \right]^{-0.45} \left[\frac{S_\nu}{f.u.} \right] \left[\frac{D}{kpc} \right]^2$$

where $\nu = 5$ GHz was assumed, the flux density ($S_{5\ GHz}$) was taken from column 5, and the electron temperature (T_e) and distance (D) were assumed to be respectively 8,000 K and 10 kpc. Using the L_c values as a function of spectral type[13] the numbers of 07 and 09 main sequence stars required to ionize these nebulae are given in columns 7 and 8 respectively.

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Infrared Photography of OH Airglow Structures

INFRARED airglow emission is bright, patchy and erratic[1,2]. The primary source of this emission was identified by Meinel[3] as rotation-vibration bands of the OH molecule. These and subsequent studies[4-6] did not delineate the true morphology of the infrared night sky because large fields of view (~ 20 deg^2) were used and only point by point measurements taken. Accurate mapping of the night sky requires a small field of view to resolve the smallest structures and a rapid scanning rate to "freeze" any time variations in the luminosity.

We have carried out a study at 2.2 μm (ref. 7), using an infrared photometer with a 1.4 square degree field of view scanning at 12 deg min^{-1}, and a similar study at 1.65 μm (ref. 8) with a 0.7 square degree field of view. At both wavelengths many small bright patches were resolved which had lifetimes of tens of minutes. During these studies, we decided to attempt to photograph the night sky with the relatively new Eastman Kodak High Speed Infrared film and a fast 35-mm camera. An f/1.2 lens was used with a Wratten 88A filter to isolate the spectral region from 7400 Å to the emulsion cutoff at 9000 Å.

Fig. 2 A 10-min exposure of the southwest sky on December 22, 1972, from 15 km west of Albuquerque (1,800 m).

Fig. 1 A 15-min exposure of the eastern sky on December 1, 1972, at Capilla Peak Observatory (2,855 m). The maximum in brightness below the centre of the frame, in spite of vignetting, is characteristic of the airglow distribution. A tree top appears above the depressed horizon.

Surprising results were obtained from a series of 60 consecutive 15-min photographs, taken during the moonless portions of the nights of December 1 and 2 at Capilla Peak Observatory (altitude 2,855 m). During this period the sky was continuously cloud-free, high flying aircraft left no enduring condensation trails, and no aureole was visible near the Sun. The photographs all show bright cloud-like structures which moved on the sky and varied in brightness. In these and about 80 subsequent photographs (taken 15 km west of Albuquerque, altitude 1,800 m) the predominant features observed in the eastern and western sky are elongated bright bands inclined somewhat to the horizon (Fig. 1). A large band moving towards the south-west horizon on December 22 is shown in Figs. 2 and 3. The patches in the southern sky seem to be more rounded and mottled (Fig. 4) than when viewed to the east or west. Before and during the exposure of Fig. 4, our 1.65 μm scanning photometer recorded an extremely bright spot in the direction of the centre of this frame. The features of Fig. 4 resemble an auroral corona, an impression exaggerated by the vignetting seen in all the photographs.

Could these cloud-like features indeed be merely clouds? We do not accept such an identification because no clouds could be detected visually anywhere in the sky during twilight or after

moonrise during these observing periods; all photographs show the sky brightness increasing toward the horizon as is expected for an emitting layer in the upper atmosphere (the Van Rhijn effect, well known to airglow observers); simultaneous photographs of the same area were taken on nights when there were clouds, with both panchromatic and infrared film. The trails of stars were modulated by the clouds and occasionally interrupted completely. No strong modulation of the star trails is present when stars pass through either the bright or dark bands which are photographed on clear nights. There is, however, a slight modulation of the star trails caused by pre-exposure, over-exposure, and vignetting effects. We conclude that these structures are indeed due to varying airglow emission and not to any type of modulation of a uniform background by atmospheric clouds, dust, or haze.

In addition to the inherent interest of being able to photograph with high angular resolution the complex airglow structures present in the infrared sky, such photographs will provide other information.

Motions of bright patches in the upper atmosphere, whether due to winds, gravity waves, or some process related to the Earth's magnetic field, are readily deduced. Assuming a height of 100 km, in accordance with the most recent direct rocket measurements[9,10], the southward component of velocity of the wide bright band near the top of Figs. 2 and 3 is about 20 m s^{-1}. On December 23, a small, bright feature in the western sky was moving due south at 43 m s^{-1}. Thus,

Fig. 3 A 10-min exposure of the same area as in Fig. 2, 30 min later. Note the motion of the broad band above the bright star trail (Fomalhaut) in the upper right. The bright stripe in the centre of the frame has elongated and moved to the right. Other variations in brightness and position of patches are apparent.

Fig. 4 A 15-min exposure on the southwestern sky from Capilla Peak on December 1, 1972. Photographs of this area were taken when an enhancement was recorded by our 1.65 μm scanning photometer. Mottled structures seem to be characteristic of the southern sky. The observatory dome and a tree top appear at the bottom of the frame.

synoptic maps of upper atmospheric "wind" speeds at the OH layer can be determined on a world-wide basis rather than relying on vapour releases from rockets or the analysis of enduring meteor trails.

Also, observations of a bright spot from two widely separated sites will yield parallax determinations of the height of the OH emitting layer; we need no longer rely on infrequent rocket measurements at a few places. Parallax measurements on different sized emission patches may yield information on the distribution of the patchiness with height and the frequency function of turbulent cell sizes.

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Fission Track Dating of the Obsidian of Lipari Island (Italy)

OBSIDIAN was widely traded in prehistoric times, and it is of particular interest to archaeologists to reconstruct the trading patterns[1-5]. One possible source of obsidian for prehistoric man is Lipari Island (Eolie Archipelago, Italy) and we have dated obsidian flows there for two chief reasons: first, to find out which of these flows could have been used by primitive man, and second, because we wished to identify the artefacts

that have been found at various sites in the Mediterranean basin.

There are three principal obsidian flows on the island of Lipari. Two of them (Forgia Vecchia and Rocche Rosse) were produced by eruptions which took place during historic times. In fact Keller[6] used the radiocarbon method for dating a palaeosoil stratigraphically below the Forgia Vecchia flow, and obtained dates ranging from 4,800 to 1,220 BP. All those who have studied the Rocche Rosse flow assign it to the volcanic event that has been dated at AD 500–550.

Fig. 1 Location of the archaeological sites investigated. 1, Monte Aquilone; 2, Catignano; 3, Fossa Cesia; 4, Lipari; 5, Filicudi.

The Acquacalda pumices enclose some obsidian pebbles. These pumices were produced in the same eruptive event, but the pebbles predate them (we have already published an age of $21,000 \pm 4,000$ years for them). Apart from these pebbles, only the Gabellotto obsidian flow may be archaeologically interesting, because of its age. Keller[7] dates it as 4,800 to 12,920 BP. These age measurements have been obtained by the ^{14}C method on sites that can be correlated stratigraphically with the flow itself.

Table 1 Dating of Lipari Obsidians

Flow	ρ_F	Φ	ρ_I	Age (yr)
Rocche Rosse	3.2	0.72×10^{15}	102,000	$1,400 \pm 450$*
Forgia Vecchia	4.2	0.99×10^{15}	160,000	$1,600 \pm 380$*
Gabellotto	26.7	0.72×10^{15}	104,000	$11,400 \pm 1,800$*

ρ_F = fossil tracks/cm^2; ρ_I = induced tracks/cm^2.

* The experimental errors include both the counting error and the uncertainty in determination of the thermic neutron dose.

The values obtained for Lipari obsidians are listed in Table 1. The high experimental error associated with the youngest samples is a consequence of the small number of fossil tracks counted. On the other hand, we thought it inappropriate to lengthen the scanning time, for these values, like those reported in the literature, mean that flows could not have been used as a source of obsidian in prehistoric times. Our results confirm the assignation of the two obsidians to the same recent event. We wish to emphasize the excellent

agreement of our results with those radiocarbon ages reported by Pickler[8] and Keller[6,7].

The source of the obsidian artefacts can be identified in several ways—for example, by studying the chemical and physical properties of the material itself[9]. We have tried to solve the problem by comparing the age of the material of the archaeological samples with that obtained for geological samples collected from the probable obsidian sources.

We have examined artefacts found on the islands of Lipari and Filicudi in order to find out which material was used in prehistoric times. The study has also been extended to artefacts from sites on the Italian Adriatic slope. The results are shown in Table 2.

Table 2 Dating of Artefacts from the Italian Archaeological Sites

Site	Sample	ρ_F	Φ	ρ_I	Age (yr)
Monte Aquilone	1	37	0.80×10^{15}	166,000	$11,000 \pm 2,900$
(Manfredonia)	3	27	0.80×10^{15}	168,000	$8,000 \pm 3,500$
	4	30	0.80×10^{15}	118,000	$12,500 \pm 5,000$
Catignano	CH 1-1	30	0.80×10^{15}	152,000	$10,000 \pm 3,000$
(Chieti)	CH 1-2	—	0.80×10^{15}	155,000	—
	F 1-2	31	0.80×10^{15}	138,000	$11,000 \pm 2,700$
Fossa Cesia	FR 2	24	0.80×10^{15}	123,000	$9,700 \pm 3,000$
(Pescara)	F 261	30	0.80×10^{15}	125,000	$11,900 \pm 2,200$
	F 2-2	36	0.80×10^{15}	150,000	$11,800 \pm 3,400$
Lipari scavo	1	27	0.67×10^{15}	106,000	$10,500 \pm 2,800$
Filicudi	1	31	0.67×10^{15}	128,000	$10,100 \pm 2,500$
	3	32	0.67×10^{15}	119,000	$11,200 \pm 3,000$

Comparing Table 1 with Table 2 we conclude that: (1) the Gabellotto obsidian was the only one used in prehistoric times on Lipari Island; this material was evidently transported by prehistoric man to the Adriatic shore of Italy; (2) the fact that the same age was obtained for samples both from the flows and from far away from the island means that the volcanic events that occurred after the artefacts left Lipari did not produce fading of tracks in Gabellotto obsidian; we have also shown this by measuring the sizes of fossil and induced tracks that have undergone the same chemical etching[12]; (3) as the identification of artefacts by the fission track method is very rapid, we believe that the study should be extended considerably to all the Mediterranean basin sites, in order to mark the geographical and chronological boundaries of obsidians that have affected the basin itself.

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Bioturbation of Superficial Marine Sediments by Interstitial Meiobenthos

IN a recently completed series of laboratory studies, lebensspuren were produced by individual macrobenthic organisms on a variety of marine sand and mud substrates (freshly collected from depths down to 30 m in the Bristol Channel), from which all other macrofauna had been removed by passing it through a 1.0 mm mesh. But the resultant tracks, trails and burrows gradually disappeared when the aquarium tanks containing them were left undisturbed after the termination of the experiments.

This effect was investigated by controlled experiments, in which macroorganisms and aerators were removed from the aquaria immediately after lebensspuren formation, and great care was taken to eliminate all extraneous vibrations. Progressive blurring of tracks and trails on both sand and mud surfaces became apparent after about 48 h, and, by the end of 10–14 day, all but the deepest marks had been obliterated (Fig. 1). Clearly, the erasure of lebensspuren was caused by small scale biogenic activity within the sediments themselves, and stereomicroscopic examination through the transparent aquaria walls invariably disclosed a copious interstitial meiofauna in the surface sediment layers.

Ostracods and nematodes were the most widely distributed and active members of the meiofaunas, but copepods, malacostracans, archiannelids and juvenile molluscs were locally abundant. The movement of sediment particles by ostracods, as viewed through the microscope, was particularly spectacular. Averaging about 0.5 mm in length, these free-ranging crustaceans were seen burrowing down at least 4.0 mm into the sediment, jostling aside sediment grains several times their own size with a vigorous, jerky motion, and disrupting the sediment fabric within their immediate vicinity. Such activity, continued over a prolonged period by a sufficiently dense population, obliterated biogenic and purely inorganic structures at and near the sediment surface. Meiobenthic copepods and malacostracans exhibited similar behaviour, but their capacities for burrowing and movement of sediment particles varied according to their size and vigour.

The activity of interstitial nematodes was different. These organisms rapidly established an intricate, closely spaced network of thread-like intergranular burrows within the surface layer of freshly emplaced sediment (Fig. 2), through which they could be observed gliding at relatively high speeds, estimated at 2–3 mm s^{-1}. The nematode burrows often persisted for several hours until obliterated by the activity of other organisms, their persistence presumably indicating reinforcement by mucus secretions. Attempts to confirm such a specific function for the abundant mucus present in the sediments by staining with thianin and mucicarmine were, however, unsuccessful. The formation of such a reticulate burrow system would undoubtedly promote downward percolation from the overlying waters into the surface sediment layer. Thus, bioturbation by interstitial nematodes and associated meiobenthos was an important factor influencing the development of a pale brown, oxidized, surface layer, 0.5–1.5 cm thick, which was observed forming within a few hours of emplacing black, anoxic muds in the aquaria. Comparable brown to reddish layers are repeatedly noted in the Challenger Expedition report[1] on deep sea deposits, and, as surfacing core and grab samples from sheltered environments on the New Zealand continental shelf and slope down to depths of at least 2,000 m, in unpublished records of the New Zealand Oceanographic Institute.

The meiofaunas observed in the laboratory all originated in shallow water deposits of the Bristol Channel. Interstitial meiofaunas are generally abundant[2-6] in littoral, inter-tidal and shallow near-shore regions; but in such high energy environments their sedimentological effects are masked by wave and current action and macrobenthic bioturbation. Nevertheless, small scale meiobenthic bioturbation, although frequently

Fig. 1 (Left) Lebensspuren made by the hermit crab, *Eupagurus*, on a surface of medium to fine sand. The broad, lunate markings were made during microphagic feeding; the lower, feathery track results from normal locomotion. (Right) The same surface after being protected from external disturbance for 12 days. Only the deepest gouged markings remain.
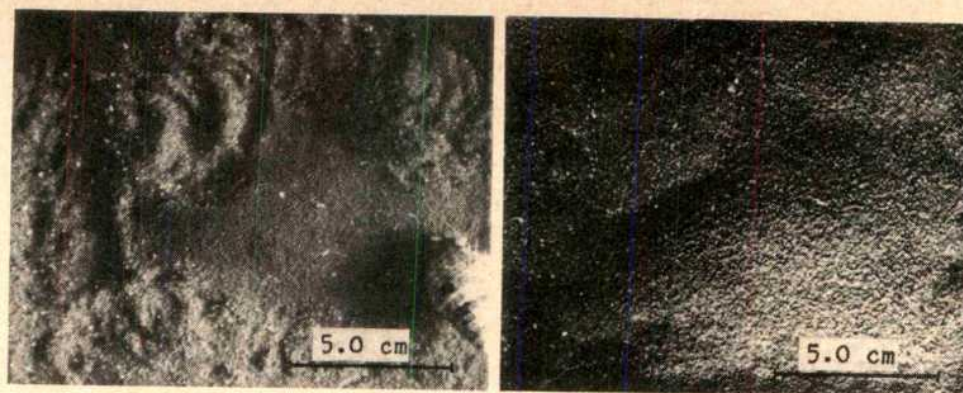
ignored, is simultaneously in progress and microenvironmentally extremely significant. Sheltered enclaves undoubtedly exist on continental shelves (for example, enclosed inlets on ria coasts and local tectonic depressions), where hydrodynamic conditions and bottom configuration are so subdued that meiobenthic bioturbation becomes a locally prominent sedimentological process.

Quantitative analyses of samples from off the east coast of the United States indicate[7] consistent numerical ratios of macro- to meiobenthos of 1:70, and wet weight ratios per unit volume of sediment of 24:1. Because the latter figure embodies no correction for factors such as molluscan shell and foraminiferal tests, it may not provide a reliable measure of the relative bioturbation potentials of the two categories of benthic organisms. But meiobenthos has a much wider dissemination than macrobenthos within the sediments, so the nature of meiobenthic bioturbation, although less obvious, is much more diffuse.

A correlation between bottom sediment composition and meiofauna distribution is frequently indicated[7–9], the larger populations usually inhabiting the coarser, sand-grade sediments. In the case of ostracods, however, Puri[9] has found that the converse applies, and he states that "the population of ostracods increases seawards with the decrease in grain-size of particles" and that "the largest populations are confined to fine-grained clastics like clays and fine silts". This disclosure is of special interest in demonstrating that the finer grained sediments, with limited intergranular pore spaces, are not invariably impoverished in meiofauna.

Wigley and McIntyre[7] noted an overall decrease in meiobenthos populations with increasing depth, although their sampling was restricted to regions shallower than 600 m. More recently, Tietjen[8] and Coull[10] have extended quantitative analyses of deep sea meiobenthos to depths exceeding 2,000 m off the east coast of the United States, Tietjen's data confirming appreciable decreases in overall numbers of meiobenthic organisms, and the complete disappearance of some meiofaunal groups, in sediments of the deeper seafloor. These findings are not entirely consistent with Thiel's[11] work on deep sea samples collected off the East African coast, in which he establishes the presence of larger meiobenthos populations at depths around 4,000–5,000 m than at 1,000 m. Further quantitative information is clearly required concerning abyssal meiobenthos, but, even if deep sea meiobenthic communities are much sparser than their counterparts in shallower waters, their bioturbational effects, in a low energy environment with low rates of accumulation, may well assume a far greater significance. Thus, even on the deep seafloor, macrobenthic lebensspuren may have to be regarded as essentially short-lived phenomena, surviving more than a few days only if conditions at the sediment surface are sufficiently abnormal to inhibit the presence of meiobenthos. It follows that meiobenthic bioturbation is a factor to be considered, in addition to the better known physical and biological marine processes, when relating lebensspuren distributions to macrobenthic population densities, either on the modern seafloor or in ancient sediments.

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Fig. 2 Intricate network of closely spaced nematode burrows in sandy mud, viewed through glass side wall of aquarium tank.

Observations on Lake Sediments using Fallout ^{137}Cs as a Tracer

SIGNIFICANT levels of caesium-137 from tests of nuclear weapons were first detected in the atmosphere in 1954; the maximum deposition[1] occurred in 1963. It would be expected that a continuously accumulating lake sediment would incorporate ^{137}Cs from fallout in a distribution pattern similar to that found from regular analysis of rain and air-borne particulate matter, provided that there has been no significant
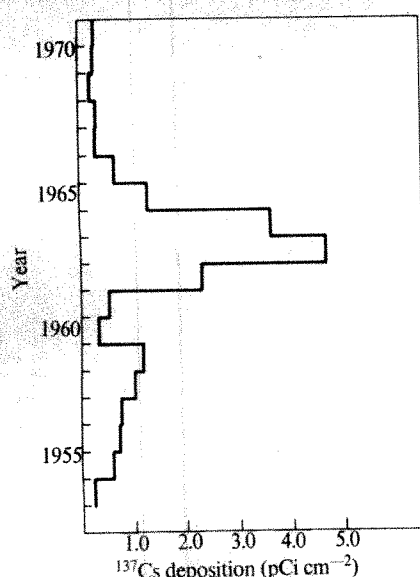
Fig. 1 Estimated annual deposition of ^{137}Cs at Windermere.

mixing in the sediment by diffusion or by the bottom fauna. Sediments from five lakes of the English Lake District have been analysed for ^{137}Cs in order to test this hypothesis (Table 1).

Table 1 Sizes and Natures of Five Lakes Studied

	Length (km)	Area (km^2)	Maximum depth (m)	Productivity Trophic status	Minimum dissolved oxygen %
Esthwaite Water	1.8	1.0	15.5	Eutrophic	0
Blelham Tarn	0.7	0.11	15.1	Eutrophic	0
Windermere	17.0	14.79		Mesotrophic	
North Basin			64		56
South Basin			42		25
Ennerdale Water	3.8	2.91	42	Oligotrophic	75
Wastwater	4.8	2.91	76	Oligotrophic	80

Cores were taken from the deepest part of each lake with a 1 m Mackereth corer[2], diameter 5.3 cm. Three replicate cores were extruded into 0.5 cm or 1.0 cm slices and combined. Samples were dried and analysed for ^{137}Cs by gamma ray spectrometry[3] using germanium (lithium) detectors. Generally each aggregate sample was counted overnight to achieve the necessary sensitivity and the lower limit of detection was then equivalent to less than 0.1 pCi cm^{-2} of sediment.

Fig. 1 shows the estimated annual deposition of ^{137}Cs by rain at Windermere, based on results for Milford Haven[1] adjusted for differences in rainfall and corrected for radioactive decay (half-life 30 yr) to the year 1971. Fig. 2 shows the distribution pattern of ^{137}Cs in the topmost 25 cm of sediment in Windermere (South Basin) and four other lakes. In Table 2 the balance of deposition between the lakes and catchment

areas is calculated. The resemblance between Figs. 1 and 2 indicates that ^{137}Cs is present in accordance with recorded annual variations in supply from rain since 1954, rather than with the cumulative deposit on the watershed. The longest profile, from Esthwaite Water, shows such good agreement with Fig. 1 that we regard this as strong evidence for the absence of significant vertical movement of ^{137}Cs after it reached the mud surface. The form of the Esthwaite distribution pattern seems to exclude either diffusion in interstitial water[4] or mixing of sediment by the bottom fauna[5] or from resuspension and redeposition of shallow-water sediment by wind-induced turbulence[6-8]. Because mixing processes would be expected to have maximum effect in the shallow and productive Esthwaite Water[9] the close resemblance of the pattern of ^{137}Cs distribution in the Esthwaite sediments to the observed pattern of annual variation since 1954 argues against the existence of significant vertical mixing in any of these lakes, and for direct deposition by rain rather than erosion from the watershed. The elongated "tail" of the ^{137}Cs curve in the two shallow lakes suggests that small amounts of ^{137}Cs may have been carried down either by diffusion or the bottom fauna.
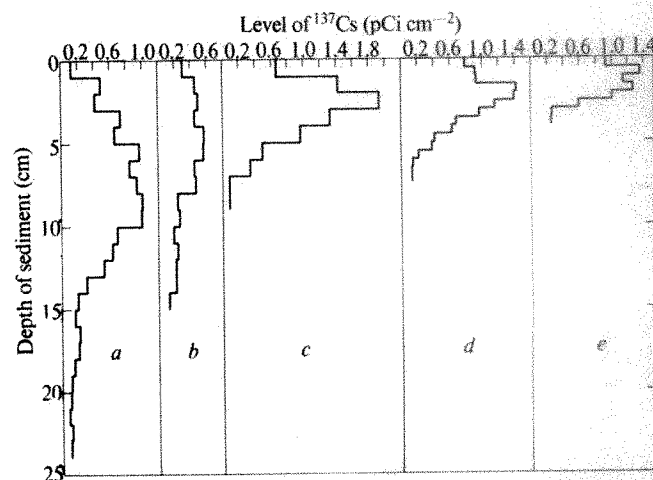
Fig. 2 Distribution of ^{137}Cs from fallout in the sediments of five lakes. a, Esthwaite Water, 1972; b, Blelham Tarn, 1970; c, Windermere, 1970; d, Ennerdale Water, 1971; e, Wastwater, 1971.

It therefore seems reasonable to accept that the position of the two horizons, the maximum deposition of ^{137}Cs in 1963 and the less precise first appearance in about 1954, indicate the depth of sediment accumulated in each lake since those dates. Table 3 shows the significantly higher accumulation rates since 1954 in the two shallow productive lakes, Esthwaite Water and Blelham Tarn, than in the deeper and less productive Windermere, Ennerdale Water and Wastwater. From work on the full sequence of postglacial sediments in these lakes[10-12] it is known, however, that the total depth of postglacial

Table 2 ^{137}Cs in Sediment and Catchment

	Total ^{137}Cs in sediment (pCi cm^{-2})	Total estimated surface deposition of ^{137}Cs by rain (pCi cm^{-2})	$\dfrac{^{137}\text{Cs in sediment (pCi cm}^{-2})}{^{137}\text{Cs surface deposition (pCi cm}^{-2})}$	$\dfrac{\text{Lake area}}{\text{Catchment area}}$	$\dfrac{^{137}\text{Cs in sediment (pCi cm}^{-2})}{^{137}\text{Cs on catchment (pCi cm}^{-2})}$
Esthwaite Water	10.7	18.5	0.58	0.059	0.035
Blelham Tarn	5.2	18.1	0.29	0.036	0.010
Windermere	7.1	16.1	0.44	0.064	0.028
Ennerdale Water	10.1	24.4	0.41	0.066	0.027
Wastwater	6.2	26.0	0.24	0.060	0.014

The estimated surface deposition by rain (column 2) has been derived from the cumulative deposition at Milford Haven[1], adjusted in proportion to the rainfall for the individual lakes as estimated from the published figures for the nearest rain gauge[21].

sediment, and hence mean annual accumulation rates over the past 10,000 yr, are much lower than these estimates based on ^{137}Cs distribution and show no correlation with these apparent differences between lakes with respect to accumulation rates since 1954 (see Table 3). The currently higher accumulation rates suggested by ^{137}Cs distribution for the two shallow productive lakes must therefore be of comparatively recent origin. Changes in populations of diatoms and invertebrates suggestive of recent eutrophication have been found in the topmost metre of sediment in Esthwaite Water[13,14] and Blelham Tarn[15-17]. Smaller changes were found in the topmost 25 cm of Windermere sediment[18] and Mackereth[19] commented on the increase in sediment accumulation rate in this lake during the past 150 yr. The question arises as to whether cultural enrichment of a lake is accompanied by acceleration of the rate of accumulation of its sediments.

Table 3 Accumulation Rates, Present and Past

	On ^{137}Cs evidence From peak in 1963 (cm yr^{-1})	From tail in 1954 (cm yr^{-1})	On palaeo-magnetic evidence from about AD 1820 (cm yr^{-1})	Mean over past 10,000 yr (full postglacial profile) (cm yr^{-1})
Esthwaite Water	0.56–1.1	0.80–0.90		0.048
Blelham Tarn	0.57–0.71	0.90–1.0		0.045
Windermere				
North Basin				0.052
South Basin	0.29–0.43	0.45–0.50	0.2	0.032
Ennerdale Water	0.19–0.25	0.40–0.45		0.058
Wastwater	0.06–0.25	0.25		0.030

The overall similarity in total depth and type of postglacial sediments in all Lake District lakes has hitherto been accepted as evidence in support of Mackereth's[20] hypothesis that, until recently, most of the organic fraction of the sediment has been derived from the drainage basin and has therefore been qualitatively and quantitatively independent of lake productivity. The much higher rates of sediment accumulation since 1954 now suggested for the two eutrophic lakes by ^{137}Cs distribution indicate the possibility that post-eutrophication sediment may differ qualitatively as well as quantitatively from older sediments.

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Crystal Structure Elucidation by the Crystal Data Centre

KNOWLEDGE of the preferred conformation of chemical groups has been shown to be essential for the determination of the structures of biological molecules. The prime example is the elucidation of the structure of the α-helix for protein molecules by Pauling, Corey and Branson[1] from knowledge that the peptide group is coplanar and the importance of the hydrogen bond, whereas others had proposed incorrect structures owing to lack of this knowledge. On a more complicated scale, because the energy stabilizing the preferred conformation is less, but on an important biological scale, it was pointed out by Canepa, Pauling and Sörum[2] that the N^+-C-C-O- group is synclinal. This was shown more clearly by Sundaralingam[3] and recently shown to be true in solution by Partington, Feeney and Burgen[4]. The conformation of this group is of great importance in nervous transmitter substances[5] and in phospholipids.

Esters are very common in biological substances and in drugs and, though it has been pointed out that esters are coplanar[5], this result has been questioned by one theoretical calculation by Kier[6] though confirmed by another theoretical calculation by Pullman *et al.*[7]. A less important example is the prediction of the structures of lysergic acid diethylamide and the hallucinogenic tryptamines and amphetamines[8] on the basis of observed crystal structure analyses of the chemical subgroups, which have been confirmed by observation[9].

The main method at present available for determining preferred conformations of organic chemical functional groups is that of statistical observation of known crystal structures. This is the reliable method used by all successful proposals of the structures of biological and chemical substances.

We have now developed a computer system for the systematic search of all known organic structures published since 1960 for chemical substructure and the calculation of the conformational parameters of the substructure. The first program of the system searches the merged Crystal Bibliographic and Data File prepared by the Crystal Data Centre in Cambridge, which was proposed by the late Professor J. D. Bernal, using an atom by atom search method for the particular group required. This program generates card images as input to our molecular geometry program (M. Dellow and P. P., in preparation) which calculates specified structural parameters of the desired group such as interatomic distances and angles, torsion angles and equations of planes with distances from the mean plane.

We have tested the system on a subset of the complete Crystal Bibliographic and Data File provided by the Crystal Data Centre in Cambridge. The subset contains 483 entries and has been searched for esters and for X–C–C–Y groups. One hundred and sixty esters were found and it can be seen clearly from these results that in all observed cases the five atoms of the ester group are coplanar. Other more extensive rules for the preferred conformations of various types of ester are also indicated. The usually observed conformation of the N^+-C-C-O groups is synclinal, though this group is sometimes observed as antiplanar in crystals[5].

The systems are implemented on an IBM 360–65/I computer. The average atom by atom search time per table entry for esters was 1.315 s and the average molecular parameter calculation

time for each ester found was 4.380 s for interatomic distances and angles, torsion angles and the equation of the plane.

Having tested the system for specific groups on a subset of the Bibliographic and Data File, we can now make searches of the complete file for the determination of the preferred conformations of many organic chemical subgroups leading to stereochemical rules allowing the reliable prediction of the conformations of many biologically important molecules and drugs.

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BIOLOGICAL SCIENCES

RNA in Coliphage T5

VIRUSES are thought to have either RNA or DNA as their genetic material, but not both[1], although oncogenic RNA viruses containing reverse transcriptase have been shown to contain some DNA. I did not expect to find that coliphage T5, a DNA-containing virus, also contained some RNA.

The bacterial strain (*Escherichia coli* F), the origin of coliphage T5$^+$, and the media and conditions for their propagation have been described, as has the method of viable bacteria count, infectious titre and metabolic techniques[2]. ^{3}H-Leucine, ^{3}H-thymidine and ^{3}H-5-uridine were obtained from Schwarz BioResearch Inc. and ^{14}C-thymidine from New England Nuclear Corp. Several preparations of ^{3}H-5-uridine were used. The purity of each preparation was ascertained by paper chromatography in three solvent systems.

Infectious T5 bands at a density of 1.54 g cm^{-3} in a caesium chloride gradient (Fig. 1, and refs. 2 and 3). When bacteria were infected in the presence of ^{3}H-thymidine or ^{3}H-leucine the radioactivity was also recovered in the same density region (Fig. 1). This was expected as bacteriophage T5 is composed of DNA and proteins. When cells were infected in the presence of ^{3}H-5-uridine, radioactivity was also incorporated into material banded in the same region as T5, and was not reduced by treatment with RNAase (Fig. 1). Electron microscopic examination of the material in the band (negative staining) revealed a preparation of uncontaminated coliphage T5. Rebanding of the ^{3}H-5-uridine-labelled virus in a second
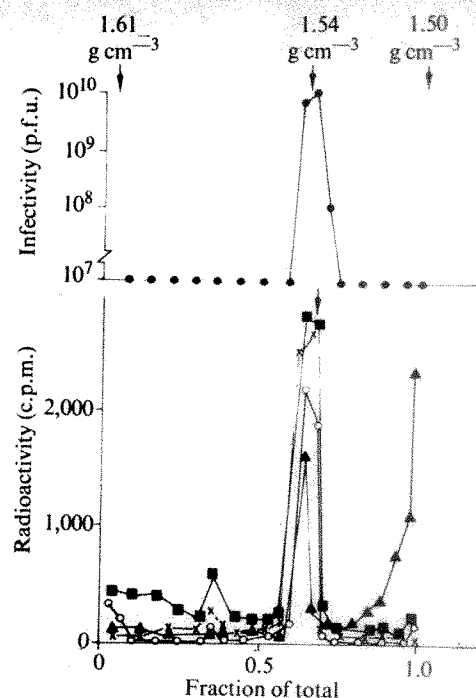
Fig. 1 Banding in caesium chloride of lysates derived from *E. coli* F infected with T5$^+$ in the presence of either ^{3}H-thymidine, ^{3}H-leucine or ^{3}H-5-uridine. Bacteria were infected with multiplicity of infection of 7, the cultures were supplemented either with ^{3}H-thymidine (3 μCi ml.$^{-1}$), ^{3}H-leucine (0.33 μCi ml.$^{-1}$) or ^{3}H-5-uridine (6 μCi ml.$^{-1}$). After 60 min aeration each culture received a drop of chloroform. Cell debris was removed by centrifugation and portions of the supernatant fluids were banded in gradients of CsCl. After equilibrium was reached, samples were collected and portions of each (10 μl) deposited on to filter disks which were analysed for acid-precipitable radioactivity[2]. Refractive indices of selected frations were determined and buoyant densities were calculated[16]. ●, Infectivity; ⊙, ▲, and ■, coliphage derived from cultures grown in the presence of ^{3}H-thymidine, ^{3}H-leucine and ^{3}H-5-uridine, respectively; ×, coliphage T5 labelled with ^{3}H-5-uridine after exposure to RNAase (5 μg ml.$^{-1}$, 37° C, 1 h).

gradient of CsCl allowed recovery of the radioactivity once more in the viral band (Fig. 2).

The head of T5 is porous[4] and so the uridine could have penetrated into the intact virus. Purified coliphage T5 was therefore incubated with ^{3}H-5-uridine for 20 h at 37° C and the preparation centrifuged to equilibrium in a gradient of CsCl. None of the radioactivity was recoverable in acid-precipitable form in any portion of the gradient. Several preparations of ^{3}H-5-uridine were used and in each case radioactivity cobanded with T5.

Nucleic acids were isolated from several preparations of purified, RNAase-treated T5 derived from cells exposed to
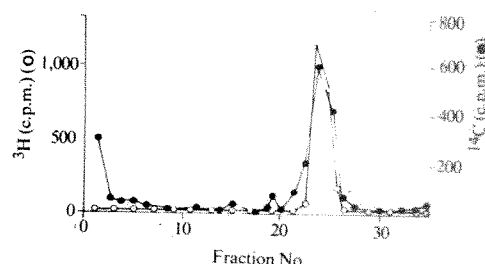
Fig. 2 Rebanding of ^{3}H-5-uridine-labelled coliphage T5 in gradient of CsCl. The peak tubes of the gradient of the ^{3}H-5-uridine-labelled T5 which had been treated with RNAase (Fig. 1) were combined, mixed with ^{14}C-thymidine-labelled coliphage T5 and run to equilibrium in CsCl. The radioactivity present in the fractions and fractive indices was determined. ⊙ and ●, Coliphage labelled with ^{3}H-uridine and ^{14}C-thymidine respectively.
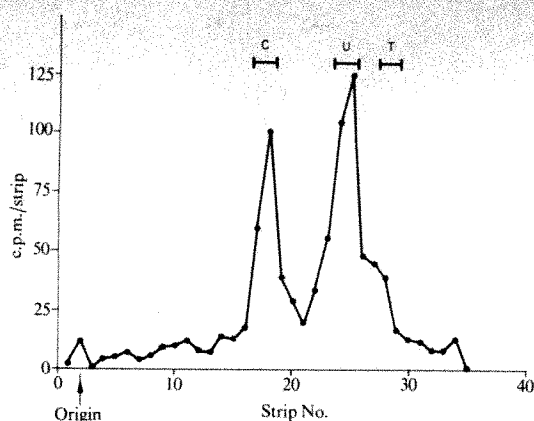
Fig. 3 Distribution of radioactivity among the bases of T5-DNA. "DNA" of T5 was hydrolysed with formic acid[17] and chromatographed on paper with isopropanol: HCl[17]. The position of the bases was detected by examination under ultraviolet light. The chromatogram was cut into strips and the radioactivity present thereon determined in a liquid scintillation counter with 10 ml. of omnifluor (4 g l.$^{-1}$ of toluene). The positions of the individual bases are indicated by lines (C, U, and T; cytosine, uracil and thymine).

^{3}H-5-uridine. The radioactivity of this "DNA" was acid-precipitable (5% trichloroacetic acid), and resistant to digestion by DNAase under conditions which allowed complete digestion of the DNA derived from T5 grown in the presence of ^{3}H-thymidine. On exposure to alkali (1.0 M KOH, 37° C, 18 h) and subsequent reprecipitation with acid, a large portion of the ^{3}H-5-uridine-labelled nucleic acid became acid-soluble, and after incubation with RNAase most of the radioactivity became acid-soluble (Table 1).

Base composition analysis of the ^{3}H-5-uridine-labelled nucleic acid (Fig. 3) showed that the radioactivity was recovered as uracil and cytosine with possibly a small amount as thymine. In a parallel experiment it was found that on hydrolysis of T5-DNA derived from bacteria grown in the presence of ^{3}H-thymidine, the radioactivity was recovered solely as thymine. On the other hand, chromatographic analysis of the ^{3}H-5-uridine-labelled DNA before hydrolysis showed that all of the radioactivity was recoverable at the origin (that is, in higher molecular weight form). Analysis of the ^{3}H-uridine-labelled T5-DNA in gradients of CsCl showed that it had a buoyant density identical to that of T5-DNA labelled with ^{14}C-thymidine (Fig. 4).

Analysis of the nucleic acids in gradients of caesium sulphate resulted in the ^{3}H-5-uridine-labelled DNA banding at the same position as the control (^{14}C-thymidine-labelled) T5-DNA. After digestion with DNAase, the control DNA no longer banded but the radioactivity of the ^{3}H-5-uridine-labelled DNA banded at a position typical of RNA (Fig. 5). This band lost its acid-precipitability after digestion with RNAase.

Table 1 Properties of ^{3}H-Labelled T5-DNA

	Radioactivity retained (c.p.m.)	
Treatment	^{3}H-5-Uridine-labelled	^{3}H-Thymidine-labelled
None	1,723	2,048
DNAase	1,689	57
RNAase	635	2,033
KOH	228	1,977

Portions of ^{3}H-labelled DNA were diluted in 0.01 M phosphate buffer (pH 7.0) such that the final radioactivity was approximately 2,000 c.p.m. 0.1 ml.$^{-1}$. Triplicate 0.1-ml. portions were then exposed to DNAase (3 µg, 37° C, 1 h), RNAase (5 µg, 37° C, 1 h) or KOH (1.0 M, 37° C, 18 h). After 1 h the enzyme-treated specimens were acidified with trichloroacetic acid (final concentration, 5%) and processed for the determination of acid-precipitable radioactivity. The sample digested with KOH was neutralized with 1 N HCl and then trichloroacetic acid added.

Our results indicate the ^{3}H-5-uridine is incorporated into the genetic material of coliphage T5, a DNA-containing virus. The alkali lability of the labelled material (Table 1) and its susceptibility to digestion by RNAase following DNAase treatment (Fig. 5) suggest that the bulk of the radioactivity was incorporated into an RNA-like material. The small amount of radioactivity resistant to RNAase and alkali (Table 1) might be due to the conversion of ^{3}H-5-uridine to cytidine and its incorporation into DNA after conversion to deoxycytidine (see Fig. 3).

I suggest that the ^{3}H-uridine is actually incorporated into an RNA-like material because of its ability after DNAase digestion to band in Cs$_2$SO$_4$ in the region of the gradient characteristic of RNA. Also this "RNA-like" material is linked to the viral DNA probably covalently because the ^{3}H-5-uridine-label of the "native" material bands in CsCl and Cs$_2$SO$_4$ gradients together with the viral DNA.

I do not know the role of this "RNA" in the viral genome, but because one of the DNA strands of T5-DNA contains five interruptions[5,6], perhaps the RNA acts to link between these DNA regions or perhaps as initiation sites for RNA polymerase.

In addition to T5-DNA, it has been reported previously that mitochondrial DNA of various origins[7-11], the DNAs of herpes simplex virus[12], *E. coli* 15$_T^{-13}$ and the colicinogenic factor E$_1$[14] have been found to be alkali-labile, consistent with the presence of RNA-like material in DNA. Also the DNA
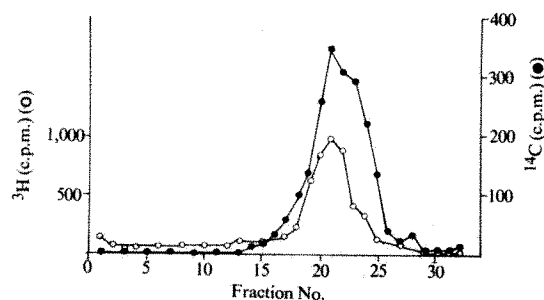
Fig. 4 Banding in CsCl of DNA derived from coliphage T5. Lysates were incubated with DNAase followed by incubation with RNAase, coliphage T5 was then purified by two successive bandings in CsCl, DNA was isolated (phenol procedure). Portions of DNAs derived from ^{3}H-5-uridine and ^{14}C-thymidine-labelled T5 were mixed and banded in a gradient of CsCl. Acid-precipitable radioactivity present in the fractions was determined.
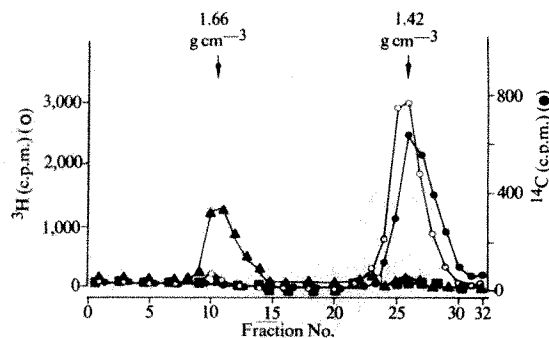
Fig. 5 Banding in caesium sulphate of DNAs derived from coliphage T5. The preparation of the DNA as in Fig. 4. ●, DNA from coliphage T5 grown in the presence of ^{14}C-thymidine; ⊙, DNA from T5 grown in presence of ^{3}H-5-uridine. The peak tubes of ^{3}H-5-uridine-labelled DNA were pooled and dialysed against 0.01 M phosphate buffer (pH 7.0) containing 2×10^{-3} M MgSO$_4$. This material was digested with DNAase (1 µg ml.$^{-1}$, 37° C, 20 min), whereupon a portion of it was incubated further with RNAase (3 µg ml.$^{-1}$, 37° C, 30 min). ▲, ^{3}H-DNA treated with DNAase; ■, DNAase-treated ^{3}H-DNA subsequently digested with RNAase. Buoyant densities were calculated[18] from the refractive indices.

of the colicinogenic factor E_1 was RNAase sensitive[14]. These results suggest that the presence of RNA in DNA may be the reflexion of a basic regulatory mechanism in DNA synthesis (ref. 15).

I am at present attempting to determine the nature of the RNA present in T5 and whether other DNA viruses contain such an RNA.

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Cell-mediated "Immunostimulation" induced by Mammary Tumour Virus-free Balb/c Mammary Tumours

PREHN has advanced the hypothesis that weakly antigenic tumours can lead to a cell-mediated response which stimulates, rather than inhibits, tumour growth[1-3]. His hypothesis was based on evidence which indicated that a low level immune reaction might enhance tumour growth. Much of this evidence came from experiments using mouse mammary tumours[1,2], although the presence of enhancing or blocking antibodies could explain many of the data[4,5]. Prehn's demonstration that low doses, but not high doses, of specifically sensitized spleen cells could benefit tumour growth in thymectomized, X-irradiated mice provided the first substantial evidence for the immunostimulation theory[8].

We have tested the cell-mediated immune stimulation hypothesis directly by using a microcytotoxicity test, which is very sensitive for measuring the effects of lymphocytes and serum from sensitized mice on tumour growth, and has been described by Hellström and Hellström[5]. Briefly, tumour cells from monolayer cultures were plated in a single cell suspension

in wells of a 'Falcon 3040 Microtest II' plate. In these experiments 500 cells were plated per well, and each test involved 8 wells. Following a 24 h incubation period, the medium and cells which had not stuck to the well surface were decanted, and lymph node cells from either normal or sensitized mice were pipetted into the wells. In our experiments the number of lymph node cells added was either 5×10^5 or 5×10^4 per well, giving a ratio of either $10^3:1$ or $10^2:1$ of lymphocytes to tumour cells plated. The plates were incubated for a further 2–3 days, and then the tumour cells which had survived lymphocyte treatment, and therefore still adherent to the surface of the wells, were washed, stained in 2% crystal violet, and counted with the aid of an inverted tissue culture microscope. The number of cells after treatment with normal lymph node cells was compared to that after treatment with sensitized lymph node cells, and the data analysed using the Students t-test.

The target tumours used were mammary tumours, free of the mammary tumour virus or any of its variants[6,7]. These tumours were derived from 2 mammary nodule lines, D1 and D2; line D1 produces only 4% mammary tumours, whereas line D2 produces 50% tumours, by one year after transplantation[6-8]. The properties and tumour potentials of these lines have been presented in previous reports[6-8]. All mammary tumours arose from D1 and D2 nodule outgrowths transplanted and maintained in untreated, virgin Balb/cCrgl female mice.

Table 1 Effect of Sensitized Lymphocytes on Syngeneic Mammary Tumours

Target tumours	No. of cells after treatment with lymphocytes from mice immunized to:		
	D1	D2	Control
D1	$25.6 \pm 3.8^*$	18.4 ± 3.5	17.3 ± 4.6
D2	6.6 ± 2.8	9.6 ± 4.0†	5.4 ± 2.8
Balb/c C3H	11.9 ± 4.1	11.3 ± 4.3	12.1 ± 3.3
Balb/c MSV‡ tumour	41.3 ± 3.5	43.1 ± 8.1	43.6 ± 12.4

$^* P < 0.0025$; % increase $= 48$%.
† $P < 0.025$; % increase $= 78$%.
‡ Molony sarcoma virus induced fibrosarcoma.

Several experiments were carried out using tumour tissue as the target cells. In the initial experiment, lymphocytes taken from mice bearing D1 and D2 tumour transplants were tested against D1 and D2 tumour cells in vitro (Table 1). Lymphocytes were used at a concentration of 100:1. Sensitized, but not unsensitized, lymphocytes enhanced the growth of specific sensitizing tumours. Growth of other mammary tumours or a MSV induced fibrosarcoma was not influenced by either type of lymphocyte.

The follow-up experiments further documented the phenomena of cell-mediated immunostimulation (Table 2). Lymphocytes were used at ratios of 1000:1 and 100:1. In five of ten experiments, stimulated tumour growth (average increase $= 48$%) was noted in the presence of sensitized lymphoid cells at a ratio of 100:1 whereas inhibition was seen in none of the ten experiments at this ratio. On the other hand, at a ratio of 1000:1, stimulated tumour growth (average increase, 52%) was seen in two of eight experiments, whereas tumour inhibition (average decrease, 50%) was seen in three out of eight experiments.

Table 2 Effect of Sensitized Lymphocytes on Syngeneic MTV-free Mammary Tumours Tested against Sensitizing Tumours

Type of tumour	No. of experiments CMI* detected		No. of experiments stimulation detected	
	$10^3/1$†	$10^2/1$†	$10^3/1$†	$10^2/1$†
D1	2/4‡	0/5	0/4	1/5
D2	1/4‡	0/5	2/4	4/5
Total	3/8	0/10	2/8	5/10

* CMI = Cell-mediated inhibition.
† No. of lymph node cells per tumour target cell.
‡ Positives occurred in passage 1 of tumour.

Several points seem to emerge; first, tumours derived from nodule line D2 seem more capable of inducing cell-mediated stimulation than do tumours from line D1 (4/5 vs. 1/5). Second, although cell-mediated inhibition was seen in three out of eight cases, this effect was seen only in first passage tumours. The tumours lost this capacity with serial passage in unsensitized Balb/c mice. For example, lymphocytes from mice bearing a D1 tumour in first passage gave a 31% decrease in tumour growth *in vitro*; in passage 3, no inhibitory or stimulatory effect, and in passage 4, a 48% increase in tumour growth. This observation suggests the importance of using primary or early passage tumours to detect a cell-mediated inhibitory response. Third, cell-mediated inhibition was only detected with a lymphocyte to target ratio of 10^3:1; stimulation was detected at ratios of 10^2:1 or 10^3:1, although more frequently with the lower ratio; and fourth, cross-reactivity was observed between D1 and D2 tumours, more frequently at doses of 10^3:1 than 10^2:1 (Table 3). It has also been seen between D1, D2 and MTV-induced mammary tumours at the higher ratio (unpublished data).

Table 3 Effect of Sensitized Lymphocytes on Syngeneic MTV-free Mammary Tumours Tested against Nonsensitizing Tumours

Sensitizing tumour	Target tumour	No. expts. CMI* detected 10:3/1†	10:2/1†	No. expts. Stimulation detected 10:3/1†	10:2/1†
D1	D2	2/5	0/8	1/5	3/8
D2	D1	0/2	0/4	2/2	0/4
Total		2/7	0/12	3/7	3/12

* CMI = Cell-mediated inhibition.
† No. of lymph node cells per tumour target cell.

Cross-reactivity suggests the presence of an organ-specific or possibly nodule-specific, rather than tumour-specific, antigen. The presence of organ-specific antigens has been postulated by Weiss *et al.*[9] on the basis of the ability of lactating mammary gland to immunize against D1 and D2 mammary tumour growth. It is of interest that they also found that pre-immunization led to enhanced growth *in vivo* of D1 and D2 tumours, a situation in keeping with the *in vitro* data reported here.

Preliminary studies show that serum taken from sensitized mice bearing D1 and D2 tumours can sometimes block the stimulation effect (G. H. and D. M., unpublished results). The experiments presented here, however, demonstrate clearly that lymphocytes from tumour-sensitized hosts can show "enhancement" or stimulation of tumour growth. These data support the hypothesis by Prehn that weakly antigenic tumours, in this case virus-free Balb/c mammary tumours (ref 9; and D. M., unpublished results), elicit a cellular immune reaction that stimulates tumour growth. The significance of this phenomenon has important implications for understanding the role of the immune system in neoplasia, and in particular for understanding such phenomena as "sneaking through", immunosurveillance, and the immunological significance of weakly antigenic tumours.

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Chromosome Pairing

IN a useful article which appeared under this title recently[1] H. L. K. W. says at one stage: "Nothing is known about the mechanism of chromosome pairing at the molecular level, but Watson and Crick (*Nature*, 171, 964; 1953) suggested that it involved the pairing of complementary nucleotide chains to form a double helix. There seems to be no alternative to this account for the specificity of pairing, and a more detailed hypothesis along these lines has been proposed by Sobell (*Proc. US Nat. Acad. Sci.*, 69, 2483; 1972)".

To me, there at least "seems to be an alternative" in the form of a model in which two homologous double helices of the Watson-Crick type are paired specifically about a dyad axis coincident with their long molecular axes[2,3].

A similar mechanism of pairing might also be involved in the formation of tertiary structure in the nucleic acid of chromosomes where repeated, perhaps particularly reverse tandem, base pair sequences occur.

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Diphtheria Toxin: Specific Competition for Cell Receptors

DIPHTHERIA toxin causes the catalytic inactivation of polypeptide chain Elongation Factor 2 when the enzymically active N-terminal fragments of toxin, particularly fragment A, are mixed with broken cells of almost any eukaryotic source[1-3] or when complete toxin molecules are incubated with intact susceptible cells[4]. Incubation of intact cells with fragment A does not lead to EF-2 inactivation. Probably, therefore, an apparatus exists in the membranes of susceptible cells that facilitates the uptake of toxin and generation of its fragment A in the cytoplasm and the entry process involves the C-terminal portion of the toxin molecule, fragment B (ref. 5).

Uchida *et al.*[6] have described the product of a mutant toxin gene, crm_{197}, a non-toxic protein of the same molecular weight as toxin which has an apparently normal fragment B but an enzymically inactive fragment A. Because crm_{197} reduces the effect of toxin on HeLa cells and yet has no effect on the reaction catalysed by fragment A *in vitro*, Uchida *et al.* suggested that crm_{197} might compete with toxin for sites on the cell membranes.

We now show by dose-ratio analysis that the inhibition can indeed be described as competitive. Typical HeLa cell dose-response curves for toxin alone and with crm_{197} are shown in

Fig. 1. As expected for competitive inhibition, the curves are similar in shape and reach the same maximum[7]. From each of several such pairs of curves, obtained with crm_{197} concentrations (I') from 1 to 32 µg ml.$^{-1}$, we determined values of toxin concentrations required to give the same response in the presence (T') and in the absence (T) of the inhibitor (Fig. 2).

The linear relationship between $\log\left(\dfrac{T'}{T} - 1\right)$ and $\log I'$, with a

slope of unity, is the result expected if toxin and crm_{197} compete for a common cellular target, because in such situations the

following relationship holds $\left(\dfrac{T'}{T} - 1\right) = \dfrac{I'}{K_I}$ (ref. 7). The intercept

indicates that the apparent dissociation constant (K_I) of the crm_{197} target complex is about 10^{-8} M.

Crm_{197} also protects rabbits and guinea-pigs against the local necrotic action of toxin injected into the skin. A very high ratio of crm_{197} to toxin is required because the skin responds to extremely little toxin and yet protection can only be significant when the crm_{197} concentration is of the same order as its dissociation constant.

In the rabbit the situation is slightly confused by a separate reaction given by these relatively high concentrations of crm_{197} alone. The normal rabbit response 2 day after the intradermal injection of 40 pg of toxin is a red patch about the same size as the bleb raised on injection (8–10 mm diameter). Larger doses give a larger red area which may have a haemorrhagic and necrotic centre. These reactions are completely suppressed by sufficient amounts of crm_{197}. But crm_{197} alone sometimes provokes a pale red ring with an internal diameter of 15–20 mm and this is intensified by toxin. In such cases, protection is more obvious two weeks after injection when the rings given by crm_{197} alone have faded.

Heat denatured crm_{197} does not protect cells in vivo or in culture against the action of toxin.
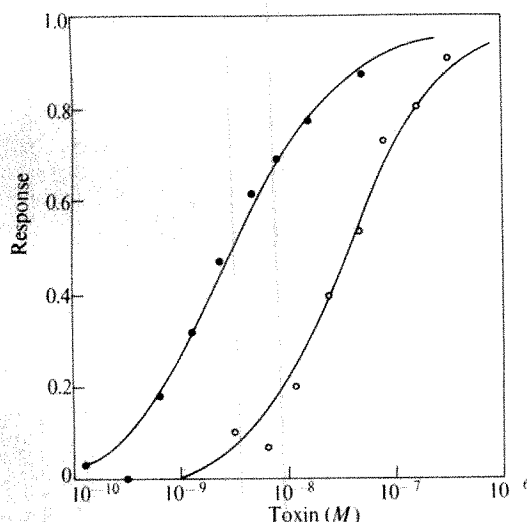
Fig. 1 HeLa cell dose-response curves for toxin (●) and toxin in the presence of 20 µg ml.$^{-1}$ of crm_{197} (○). Cells growing exponentially in spinner culture were collected by centrifugation and resuspended to 5×10^5 cells ml.$^{-1}$ in Eagle's Minimum Essential Medium supplemented with 2% foetal calf serum. 1.5 ml. aliquots of the suspension were measured into 15 ml. plastic conical tubes (Falcon) containing various amounts of toxin and crm_{197} and incubated in a 37° C water bath with moderate shaking. After 2.5 h, 0.5 µCi of [^{14}C]-L-leucine (312 Ci mol^{-1}) was added to each tube. One hour later the cells were chilled, collected on glass fibre filters and washed with 0.15 M NaCl to remove serum proteins and then with 5% trichloroacetic acid. The filters were dried and counted by liquid scintillation. The response of cells was computed as $(C-C')/C$ where C' is c.p.m. incorporated in the presence of toxin and C the control in the absence of toxin. C was generally about 7,000 c.p.m. incorporated per hour and this rate of incorporation was constant for at least 4 h after the cells were transferred to plastic tubes, even though they tended to settle.
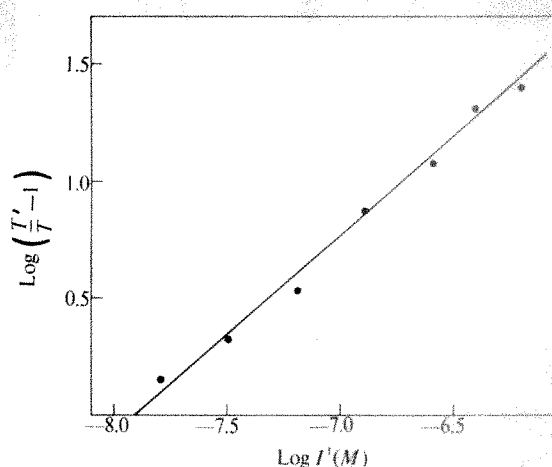
Fig. 2 Schild plot of the antagonism by crm_{197} of the action of toxin in HeLa cells. Dose ratios (T'/T) were calculated at response level 0.4 from pairs of dose-response curves such as those shown in Fig. 1.

All these observations might also be explained if crm_{197} acted, not as a competitive inhibitor, but by combining with toxin and neutralizing it[9]. We consider this neutralization unlikely because crm_{197} does not inhibit the enzymic action of fragment A in vitro; dimers[10] and higher aggregates of toxin are toxic; and a mixture of 10^{-7} M toxin and 4×10^{-6} M crm_{197}, at which concentration there would be almost complete protection in HeLa cell cultures, produces a response in rat skin indistinguishable from that with toxin alone. Rat cells seem to lack the specific mechanism for toxin uptake existing in sensitive cells and yet can be intoxicated by comparatively very high concentrations of toxin which appears to enter cells very slowly[3] by a non-specific route (T. J. and J. M. Moehring, personal communication).

Thus, we believe that the present evidence shows true competition between toxin and crm_{197} for some cellular receptor. The results do not locate the receptor unambiguously but it is clearly most likely to be a component of the cell membrane involved with the initial binding of toxin or its subsequent entry into the cytoplasm. Because fragment B is necessary both for entry and for competitive inhibition, it is reasonable to suppose that the binding of toxin or crm_{197} to the receptor occurs primarily through fragment B. Thus, the dissociation constant, about 10^{-8} M, found for crm_{197} would be identical to that of toxin itself. A constant of this magnitude would explain the level of the so-called "saturating dose" of toxin, the lowest concentration that gives the most rapid inhibition of protein synthesis in tissue culture cells. For HeLa cells this is about 2–3×10^{-8} M (refs. 11, 12) at which most of the receptors would be occupied and the addition of more toxin could have little extra effect.

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Senescence of Human Cells in Culture

DR L. K. BLEYMAN[1] need not be concerned that our experiments on clonal senescence of human cells in culture are being carried out in ignorance of earlier studies of such ageing in protozoa. Indeed the paper he cites[2] refers to one important study carried out with protozoa. The experiments with human cells are derived directly from earlier work with simple eukaryotic organisms such as fungi. When the first results were being prepared for publication[3], reference was made to related studies with ciliated protozoa and a copy was sent to Professor T. M. Sonneborn for comment. In subsequent correspondence with him it became clear that it would not be possible (in a paper limited in length by the editor of *Nature*) to do justice to the many important observations on the complex interaction between nuclear and cytoplasmic degenerative changes during ageing in these organisms. It would be most valuable if Dr Bleyman could now be persuaded to publish a review of these experiments in the light of subsequent biochemical studies on the mechanism of clonal senescence in other organisms.

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Circadian Variation of the Lethality of Methadone

Lenox and Frazier[1] have reported the discovery of a circadian variation of methadone tolerance in rats. Their claim hinges on an observed survival of nine out of twenty-six rats (34.6%) injected at 0500 h compared to an average survival of only 17.3% for similar groups injected at five other times of day. But their use of the χ^2 test is incorrect and the experimental results do not support the hypothesis that the circadian cycle influences the tolerance to methadone.

To calculate the significance of the observed variation of survival percentage with time of injection it is necessary to recognize that survival statistics in experiments with small groups are neither Gaussian nor Poisson, but are binomial[2]. Whenever an experiment with a group of size n has only two possible outcomes (such as survival and death) with probabilities p and q ($q = 1 - p$) the probability of x survivals is given by

$$P(x) = n!(x!(n-x)!)^{-1}p^x q^{n-x}$$

The best estimate of p, under the null hypothesis that the survival rate is independent of time of injection, is defined by the observed survival of 31 animals out of the 153 used in the programme of six experiments. Therefore $p = 0.203$ and $q = 0.797$. The binomial function based on these values for p and q, with $n = 26$, as for the group at 0500 h, is shown in Fig. 1. The sum of the ordinates from $x = 0$ to $x = 8$ is equal to 0.936
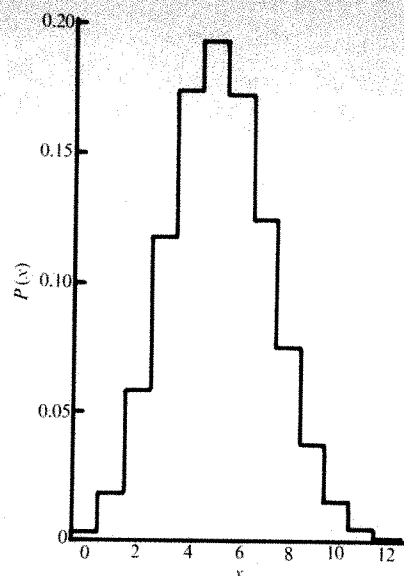
Fig. 1 The binomial function for $n = 26$ and $p = 0.203$.

and therefore the likelihood of 9 or more survivals is 6.4% in this one group. But there were five other groups, any one of which could have produced an interesting result. The probability of obtaining eight or fewer survivals in all six groups is equal to the product of the six separate probabilities. There are only two distinct probabilities to consider: 0.936 for $n = 26$ in three experiments and 0.950 for $n = 25$ in the other three. The overall probability that $x < 9$ is therefore $0.936^3 \times 0.950^3 = 0.703$. It follows that there will be a 29.7% chance that $x > 8$ in at least one of the six groups, and the null hypothesis is compatible with the observations.

Statistical interpretation of the results of this experiment is complicated by the fact that previous work cited by Lenox and Frazier had suggested that survival would be greatest at 0900 h, only one time interval away from the 0500 h group. If the work is repeated it will require only eight survivals at 0500 h or 0900 h to rule out the null hypothesis.

Unless there are compelling biological reasons for using an LD_{80} dose of methadone the sensitivity of the experiment can be doubled by employing the drug at the LD_{50} level.

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Attraction of *Spodoptera littoralis* Larvae to Colours

DURING a research programme on phagostimulants[1-3] for the larva of the Egyptian cotton leafworm, *Spodoptera littoralis* Boisd., it was found that their incorporation into poison baits did not sufficiently improve the latter's attractivity. Further stimuli, for example optical ones, seemed to be needed. We therefore determined the influence of edible colours, similar to those used in studying boll weevil attraction[4], on the feeding rate of *S. littoralis*. A range of commercial food colours of the 'Edicol Supra' and 'Edilake' ranges (Imperial Chemical Industries, England), now produced under the label of 'Certicols' and 'Certolakes', respectively (Williams (Hounslow) Ltd), were tested. The 'Edilake (Certolake)' colours are aluminium lakes containing a high proportion of alumina as extender of the corresponding 'Edicol Supra (Certicol)' dyes, which are sodium

Table 1 Colour Attraction in Phagostimulation Trials with *Spodoptera littoralis* Larvae

No.	Hue	Methuen notation*	Name of colour	Feeding ratios† at dye concentration tested 1%	0.25%
1	Yellow	2A6	'Edicol Supra Tartrazine NS'	0.96	2.1
2	Yellow	3A4	'EdilakeTartrazine NS'	1.9	2.1
3	Yellow	3A4	'Edilake Yellow FCS'	3.3	2.0
4	Orange yellow	4A6	'Edicol Supra Yellow N'	0.61	2.4
5	Orange	5B2	'Certolake Plain Chocolate Colour 175290'	2.1	
6	Orange	5B3	'Certolake Milk Chocolate Colour 175285'	1.8	
7	Orange	6A6	'Edicol Supra Yellow FCS'	0.65	4.9
8	Reddish orange	7A5	'Edicol Supra Orange AG'	1.1	2.2
9	Red	9A5	'Edicol Supra Ponceau 4RS'	0.25	0.94
10	Red	10A4	'Certolake Ponceau 4R'	1.4	
11	Red	11B4	'Edicol Supra Carmoisine WS'	0.55	0.93
12	Red	11B5	'Edicol Supra Raspberry A'	0.77	1.1
13	Bluish red	12B5	'Edicol Supra Amaranth AS'	0.34	0.84
14	Bluish red-purplish red	12C3	'Edicol Supra Blackcurrant A'	0.44	1.4
15	Purplish red	13A6	'Edicol Supra Erythrosine'	0.25	0.36
16	Purplish red	13A5	'Certolake Erythrosine'	0.76	
17	Purplish red	13-14B4	'Certolake Amaranth'	1.4	
18	Blue	21B4	'Edicol Supra Blue XS'	0.6	0.59
19	Blue	22A4	'Certolake Indigo Carmine'	1.3	
20	Blue	23A7	'Edicol Supra Blue EGS'	0.16	0.41
21	Turquoise	24C8	'Certicol Green S'	2.3	1.7
22	Green	27B4	'Certolake Green 172257'	4.4	1.7
23	Green	27B4	'Certolake Green 172679'	2.1	

* The colour of 'Edicols' and 'Certicols' was determined according to the *Methuen Handbook of Colour*[5], on 'Styropor' lamellae painted with 0.25% of the dye, whereas 'Edilakes' and 'Certolakes' were determined at 1%.

† The ratio of weight 'Styropor' consumed in choice trials (lamellae treated with dyes+3% sucrose tested against lamellae treated with 3% sucrose alone) is recorded in the last two columns, feeding ratios. The average total consumption on two lamellae in these experiments was 8.6 mg.

salts. 'Edilakes' are used mainly when water-soluble food colours would be unsuitable, for example in fatty or oily media, and contain generally from 15 to 25% of the corresponding 'Edicols'.

To assess phagostimulation, we used the 'Styropor method'[1]; lamellae (6×3 cm) of 'Styropor' (foamed polystyrene) of density 0.016 (P_{16}), with dry sucrose residues as phagostimulant,
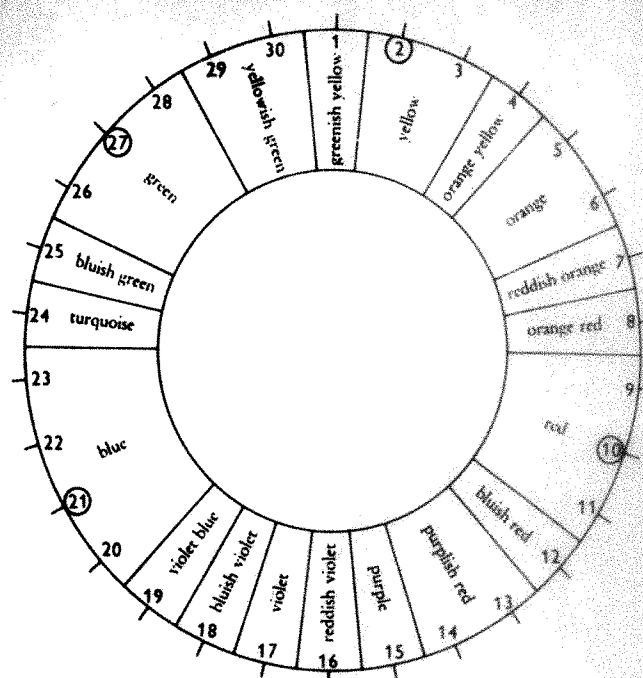
Fig. 1 The colour circle[5]. The numbers which represent the four primary colours have been ringed.

were offered in large Petri dishes (15 cm) to larvae of *S. littoralis* weighing 170-190 mg, under ordinary day-and-night conditions of illumination and at 27° C. In this study the lamellae were painted with varying sucrose and dye concentrations in water-ethanol 9:1, containing one drop of 'Triton X-100' per 10 ml. of solution as spreader, and were left to dry for 24 h. Both choice trials (two differently treated lamellae per dish) and no-choice trials (only one lamella per dish) were conducted. The weight of 'Styropor' consumed per larva served as criterion of phagostimulation, the results being recorded after 48 h.

In choice trials between lamellae treated with 3% sucrose plus varying concentrations of dyes compared with 3% sucrose only, it was found that the larvae feed more strongly on certain of the coloured lamellae (Table 1). In fact, all the colours lying in a semicircle, ranging clockwise from turquoise (24) to reddish orange (7) in the colour circle (Fig. 1), enhanced phagostimulation; this is the area around the primary colours green and yellow[5]. Colours lying within the other half of the colour circle (around the primary colours red and blue) were inactive or even repellent (Table 1).

In the attractant colours, colour intensity also played a role: colours which are too intensive were less attractive. Activity was therefore mostly higher with 'Edicols' at 0.25% than at 1%;

Table 2 Choice Trials with Two Yellow and One Green Colour

	Dye		Sucrose	*versus*	Dye		Sucrose	Feeding ratio
A	1% 'Edilake Yellow FCS'	+	3%		1% 'Edilake Tartrazine NS'	+	3%	1.0
	1% 'Edilake Yellow FCS'	+	3%		1% 'Certolake Green 172257'	+	3%	1.8
	1% 'Edicol Supra Tartrazine NS'	+	3%		1% 'Certicol Green S'	+	3%	1.8
B	1% 'Edilake Yellow FCS'	+	3%		—		5%	0.96
	1% 'Edilake Yellow FCS'	+	3%		—		6%	0.65
	1% 'Edilake Yellow FCS'	+	3%		—		7%	0.57
	1% 'Edilake Yellow FCS'	+	3%		—		8%	0.56
	1% 'Edilake Tartrazine NS'	+	3%		—		5%	0.96
	1% 'Certolake Green 172257'	+	3%		—		5%	1.0
	1% 'Certolake Green 172257'	+	3%		—		8%	0.51
	Controls:	—	3%		—		3%	1.0
		—	3%		—		5%	0.52
		—	3%		—		8%	0.33

A: Colour + 3% sucrose against another colour + 3% sucrose.
B: Colour + 3% sucrose against varying concentrations of sucrose.

the 'Edilakes' were highly active at 1% as they contain only a quarter or less of the corresponding 'Edicol'.

In choice trials between yellow and green colours applied on sucrose-treated 'Styropor' lamellae (Table 2, A), two 'Edilake' yellow colours, 'Yellow FCS' and 'Tartrazine', were equally active, but much more attractive than 'Certolake Green 172257'. This is interesting because in no-choice experiments this green dye was consistently more attractive than the yellow lakes. As 'Certolake Green 172257' is a mixture based on 'Certicol Green S' and 'Certicol Tartrazine S' ('Edicol Supra Tartrazine NS'), we tested these two constituents against each other. The yellow colour was again the more attractive.

Sucrose (3%) with 1% of 'Edilake Yellow FCS', 'Edilake Tartrazine NS' or 'Certolake Green 172257' were about equally phagostimulatory to 5% sucrose (Table 2, B), resembling Wiesmann's classical red hue colour experiments[6] (water-wettened red filter paper disks were as attractive to houseflies as 1–5% sucrose solutions soaked into white filter paper disks). The table also shows that 3% sucrose was half as active as 5%, but when fortified with 1% dye it was half as active as 8% sucrose.

Table 3 No-Choice Trials with Yellow and Green Colours

Sucrose		Colour	'Styropor' lamella consumed mg/larva
3%	+	1% 'Edilake Tartrazine NS'	7.2
—		1% 'Edilake Tartrazine NS'	1.1
3%	+	1% 'Edilake Yellow FCS'	5.2
—		1% 'Edilake Yellow FCS'	0.4
3%	+	1% 'Certolake Green 172257'	9.6
—		1% 'Certolake Green 172257'	0.7
3%		—	6.8

The approximate equality of attraction between 5% sucrose and 3% sucrose with 1% of either of the two yellow dyes or the green dye does not imply that 1% of the dyes alone is equivalent as phagostimulant to 2% sucrose; they are non-phagostimulatory alone at this concentration (Table 3). This could also be inferred from observations every 10 min in 5-h-long choice experiments, during which the frequency larvae stayed on either the 1% 'Edilake Tartrazine NS' or the 3% sucrose lamella was determined. Larvae stayed about twice the time on the 'Edilake Tartrazine NS' as on the sucrose lamellae, but fed almost exclusively on the latter. The dye seems thus to be an arrestant[7] for larvae of S. littoralis. This conclusion is supported by the finding that the positive bias conferred by 1% 'Edilake Tartrazine NS' to 3% sucrose, compared to 3% sucrose alone, disappears when such choice experiments are conducted in complete darkness.

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Vascular Permeability Factor: Dissociation from the Angiotensin II Induced Pressor and Drinking Responses

THE parenteral administration of saline extracts of renal tissue to nephrectomized animals of various species causes protracted elevation of blood pressure, increased drinking, formation of ascites and pleural effusions, and arteriolar necrosis[1-7]. While renin has been implicated in pathogenesis as it is a major component of saline renal extracts, the mechanisms producing these various phenomena and their interrelationship remain unclear. It has been postulated[5,6] that the blood pressure response is due to angiotensin II generated by the renin-rich extract and the effusions caused by changes in vascular permeability induced by the blood pressure elevation. Asscher[7], however, suggested that another factor of renal origin was involved which increased vascular permeability to plasma proteins.

Considerable evidence has already been accumulated to support the theory that excess renin, by angiotensin formation, is vasculotoxic. Animals with renal artery clipping who develop malignant hypertension do have excessive renin and aldosterone secretion[8], and the simultaneous administration of these hormones can produce devastating vascular injury and serous effusions[9]. Furthermore, diffuse myocardial and renal lesions can be produced by administration of large doses of angiotensin[10]. The vasculotoxicity of renin is also suggested by its presence in excessive amounts in human malignant[11] and renovascular hypertension and by the direct relationship between peripheral plasma renin activity and vascular complications in patients with essential hypertension[12].

The recent synthesis of a highly specific peptide competitive inhibitor of angiotensin II, Sarcosine[1] Ala[8] angiotensin II[13] enables investigation of vascular permeability subsequent to intraperitoneal injection of crude renal extract in the presence of angiotensin blockade. We used this approach to clarify the role of excess renin and angiotensin in causing vascular permeability.

Female Wistar rats (295 to 325 mg) were bilaterally nephrectomized. The femoral vein was cannulated for infusion
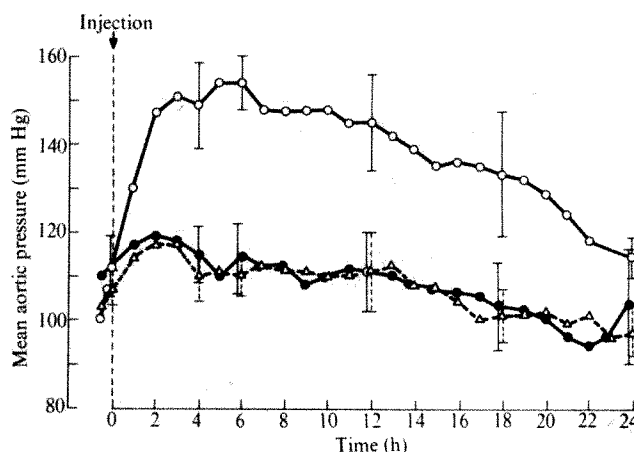
Fig. 1 Infusion of an angiotensin II inhibitor in nephrectomized rats completely blocked the characteristic protracted pressor response induced by the intraperitoneal injection of crude renal extracts. (Mean ± s.d.) (○—○, Renal extract; ●—●, renal extract and inhibitor; △ - - - △, saline.)

and the external iliac artery for constant blood pressure monitoring while the animal was awake and drinking. The kidneys were homogenized with 5 ml. of 0.9% saline in a 'Vertis' blender, and the homogenate was centrifuged at 5,000 r.p.m. for 10 min. Two gram liver aliquots obtained from other animals were similarly prepared. Following blood pressure stabilization, 3.5 ml. of either saline (N-6), or the supernatant from the renal extract (N-5), or liver extract (N-8) was injected intraperitoneally with a blunt needle.

In an additional six animals, intravenous infusion of the angiotensin inhibitor at 4 μg min^{-1} completely blocked the pressor response to an intravenous dose of 100 ng angiotensin II. Kidney extracts were then injected and the infusion of the blocker was continued throughout the study. Complete blockade of the pressor effect of intravenous exogenous angiotensin II was reaffirmed at 4, 12 and 24 h.
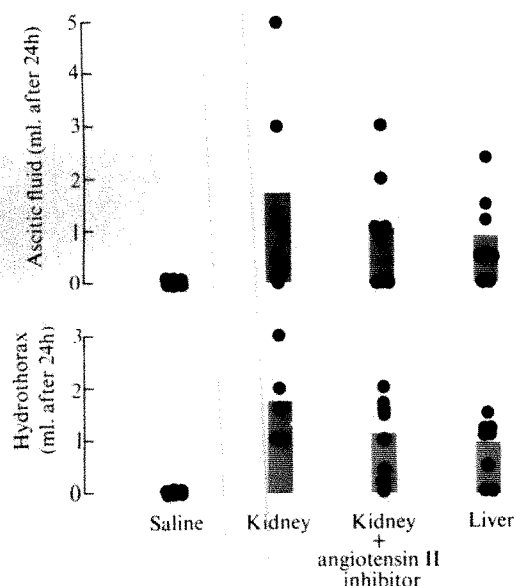
Fig. 2 Intraperitoneal injections of either crude renal or hepatic extracts produced pleural and abdominal effusions in nephrectomized rats. Concurrent infusion of the angiotensin II inhibitor did not prevent the fluid accumulation produced by the renal extracts.

Intraperitoneal administration of the crude renal extracts produced an immediate and sustained rise in blood pressure (Fig. 1) which was significantly elevated above control in 1 h ($P < 0.01$). Blood pressure reached peak levels at 6 h (154 ± 4.5 mm Hg s.d.) and then fell slowly over the remaining 24 h period. In contrast, in animals given the saline injection, the blood pressure did not rise significantly above baseline. The pressor response of the crude renal extract was totally abolished in animals receiving infusion of the angiotensin II inhibitor.

A second effect of the crude renal extracts was to stimulate drinking. The fluid intake over the 24 h period (31 ± 10 ml. s.d.) in these animals was significantly greater ($P < 0.01$) than in the animals with the saline injection (10.4 ± 6.0 ml.) or those given the liver extract (10 ± 5.3 ml.). Increased drinking was similarly abolished by administration of the angiotensin II inhibitor. Fluid intake in the animals given the inhibitor and the crude renal extract (15.8 ± 4.4 ml.) was not significantly different from either the control saline group or the group given liver extract.

In contrast, the induction of serous peritoneal and pleural effusion was not suppressed by the angiotensin inhibitor (Fig. 2). Thus, this response does not seem to be the result of the pressor action of the generated angiotensin II. Heterologous liver extract studies enable the pressure response to be dissociated from the production of serous effusions. Although the liver extracts caused neither hypertension nor

drinking, they did produce serous effusions in seven of eight animals.

Our results confirm that the hypertension and drinking responses in nephrectomized rats after intraperitoneal injection of renal extracts are mediated by the generation of angiotensin II as they were both entirely abolished by a specific angiotensin II inhibitor. In contrast, it does not seem to be the factor involved in the production of serous effusions, the so-called vascular permeability factor; effusions occurred during angiotensin blockade and were also caused by liver extracts. Although production of severe hypertension in rats may be associated with areas of constriction and dilatation of small arteries resulting in sequestration of plasma proteins beneath the endothelium[14], an elevated blood pressure *per se* was not a prerequisite for serous effusion formation and no vascular lesions were found on histological examination. We suggest that the occurrence of serous effusions observed in animals receiving renal extracts is not dependent on hypertension-induced vascular damage.

Our results agree with those of Giese[4] and Nairn[3] in which angiotensin II infusions did not produce a serous effusion to the same extent as intraperitoneal injection of renal extracts in nephrectomized rats. Suggestions that the effusions are due either to an unidentified renal substance causing changes in vascular permeability[7] or to a renin effect other than generation of angiotensin II[6] are rendered less likely by our findings of similar effusions after injection of liver extracts. They are more likely to be due to a non-specific effect of tissue proteolytic enzymes and other products injected into the peritoneal cavity. Furthermore, Asscher[15] has demonstrated that non-pressor placental extracts also produce serous effusions.

Angiotensin II can produce vascular injury[16], but the pleural or peritoneal effusions often observed after injection of renal extracts[2–7] or with bilateral ureteral occlusion[17] do not seem to be a specific consequence of its action. On the other hand, our study reaffirms the specificity of angiotensin II as the pressor and polydipsic agent occurring in renal extracts.

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Liquid Crystals in Human Bile

GALLSTONES may grow from microspheroliths, non-crystalline associations of cholesterol, pigment or calcium carbonate[1,2]; these spherical structures have been observed to aggregate and crystallize, but their composition and nature have never been well defined.

Bourges *et al.*[3] and Admirand and Small[4] have largely excluded para-crystalline phases in the mechanism of cholesterol precipitation. The results of Admirand and Small[4] suggest that human bile is either a one or two phase system (micellar solution or micellar solution plus crystalline cholesterol). A stable three-phase system (crystalline, liquid crystalline and micellar) could occur at unusually high lecithin concentrations. When the maximum cholesterol solubility limit has been exceeded therefore, crystalline cholesterol is expected to precipitate from bile.

We have observed as much cholesterol above saturation in normal, non-gallstone associated, biles as in patients with cholelithiasis, yet only the latter group may have solid crystals. We therefore re-examined the morphology of biliary precipitates, particularly the formation of birefringent particles as detected by polarizing microscopy.

Eleven cholesterol gallstone-associated samples were studied soon after collection with the temperature maintained at 37° C; other specimens had been stored at $-20°$ C. In all, twelve specimens of normal bile and forty-six of gallstone-associated bile were examined.

The birefringent particles seen were of two types. Small solid crystals in the form of parallelepipeds (cholesterol crystals) were found in fresh lithogenic specimens and stored specimens of normal and abnormal samples. Also, birefringent droplets with a diameter of about 5 μm were frequently observed, which decreased in number on heating from room temperature to 37°–40° C, and disappeared completely at even higher temperatures.

The droplets often formed clusters as shown in Fig. 1. Large birefringent areas formed from slow coalescence at room temperature (Fig. 2). Occasionally, areas with a pseudo-isotropic texture developed which were optically positive uniaxial. The batonnets in Fig. 3 resulted from rapid cooling of a sample which had been heated to 80° C. These features indicate a liquid crystal state with a lamellar structure[5-7]. Liquid crystalline mesophases have been reported in other body fluids and normal tissues, for example, plasma of humans with hyperlipaemia[8] and biliary obstruction[9]; and adrenal cells, ovary and muscle[8].

To verify the liquid properties of the droplets, some samples were passed through a 0.025 μm pore size microfilter. As the filtrate still contained droplets of much larger diameter, these can be deformed and flow through very narrow openings.
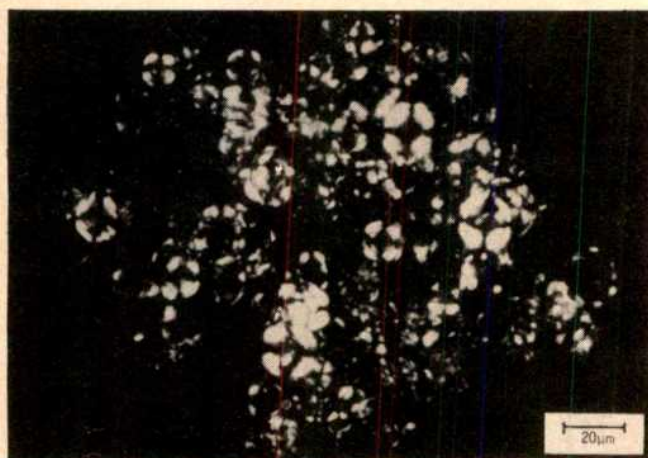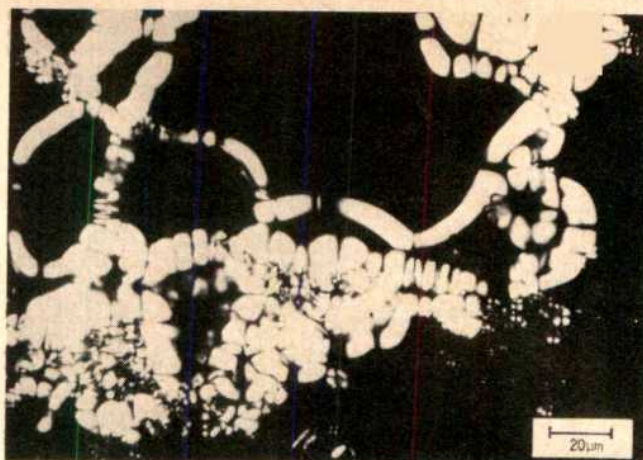
Fig. 2 Extended liquid crystalline areas. 23° C, crossed polarizers.
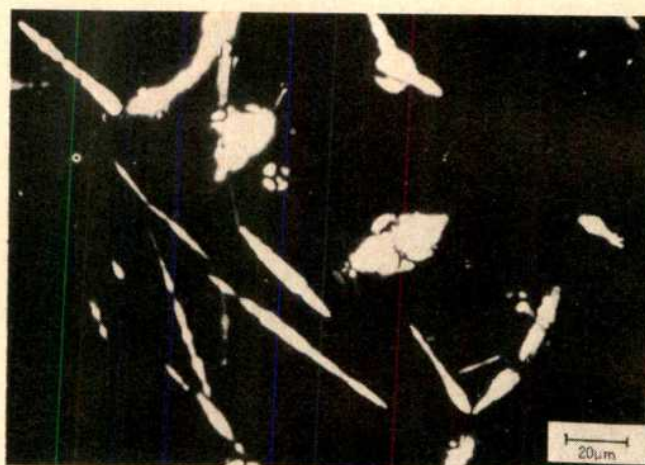
Fig. 3 "Batonnets" obtained by heating to 80° C and successive cooling. 23° C, crossed polarizers.

We observed liquid crystals in eleven fresh lithogenic biles and twenty-four stored bile samples of which five were normal and nineteen were associated with gallstones. All samples were saturated or supersaturated with cholesterol (saturation defined in ref. 10). In the detailed study on human bile by Admirand and Small[4], microscopic observations were confined to the centrifugation sediment, in which only solids were found. This would be expected in view of our observation that the liquid crystals are less dense than bile and, therefore, float on centrifugation.

The liquid crystalline state in human bile seems not to be stable. Sequential microscopic observations of human biles maintained at 37° C for as long as two weeks showed that the liquid crystal particles slowly disappear and cholesterol crystals form in compensation. They completely disappeared in a sample that initially showed only liquid crystals, for example, within 72 hours after incubation at 37° C, and cholesterol microcrystals were formed instead.

As the composition of the liquid crystals has not been determined, their role in gallstone formation cannot yet be defined. We suggest that the cholesterol concentration in the liquid crystalline phase is considerably higher than in the surrounding isotropic phase, and the presence of liquid crystals inhibits the precipitation of excess cholesterol in a solid crystalline form by delaying its nucleation. This would result from reduction in cholesterol supersaturation in the micellar phase by the formation of a liquid crystalline portion with a relatively high cholesterol concentration.

A stabilizing influence of liquid crystals depends upon their more rapid nucleation than solid crystals. We observed only

Fig. 1 Liquid crystal spherulites, untreated human bile at 23° C, crossed polarizers.

liquid crystals in fresh specimens of human bile, which supports this hypothesis. The small size of the liquid crystals suggests simultaneous nucleation at a large number of sites. A rapid change from a stable to an unstable solution leading to multiple nucleation could result from diurnal variations in the composition of hepatic bile both in man[11,12] and in other primates[13]. Liquid crystals in human bile may thus play an important role in the transition from the non-lithogenic to the lithogenic state. Further studies of this complex and dynamic system are necessary in regard to compositional changes and time scales.

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Toxicology of Fluoro-olefins

THE often surprising toxicity of several of the fluorinated organic compounds is well known[1]. A number of rather diverse structural types have been found to impart high toxicity although seemingly closely related types have been found to have rather low toxicities. Unfortunately, this varied behaviour of fluorinated compounds has occasionally become tragically established. While the *modus operandi* is now known for types such as monofluorides[2], phosphofluoridates[3], and active halogen compounds, for example, α-haloketones, much less is understood about fluorinated alkenes[4].

This toxicity, or lack of it, has seemed to be bestowed upon fluoro-olefins in a random fashion. Attempts to correlate trends in toxicity with increasing fluorine substitution by ascribing olefin hydrolysis to hydrogen fluoride have not been entirely satisfactory. For example, perfluorobutene-2 and perfluoroisobutylene are isomeric, but although the toxicity of perfluoroisobutylene is well known, perfluorobutene-2 is not considered especially dangerous. Also, chlorotrifluoro-ethylene is about forty times more toxic than tetrafluoro-ethylene, and perfluoroisobutylene is about ten times as toxic as phosgene although both would be expected to be similar if hydrolysis were the only causative agent. One particularly interesting finding is the three-fold higher toxicity of *trans*-2,3-dichlorohexafluorobutene-2 over that for the *cis* isomer[5].

Table 1 Olefin Toxicities

Olefin	LC$_{50}$, p.p.m. (4 h exposure)	ALC, p.p.m.
$CH_2=CHF$		800,000
$CH_2=CF_2$		128,000
$CF_2=CF_2$	40,000	
$CH_2=CCl_2$	32,000	
$CHCl=CCl_2$		8,000
$CCl_2=CCl_2$		4,000
$CF_3CF=CF_2$	3,000 (3,240 to 13,365; 2 h)	
$CF_2=CFCl$	1,000 (7,560; 2 h)	
$CF_2=CCl_2$		1,000
$CF_3CF=CHCF_3$		200
$CF_3CCl=CClCF_3$		100
trans	(61; 1 h)	
cis	(179; 1 h)	
$(CF_3)_2C=CF_2$	0.76	

Chiefly from refs. 4, 9 and 10, LC$_{50}$, lethal concentration for 50% of animals, 4 h exposure. ALC, approximate lethal concentration, 4 h exposure.

Little systematic attention has been directed towards determining comparative toxicities, for example LC$_{50}$ or ALC concentrations, for this type of compound, but we have collected some of the available data in Table 1.

It is clear from descriptions of physiological effects of these olefins that they do not act by a simple physical mechanism but rather by some biochemical interaction. Central nervous system involvement is often observed, particularly when these compounds are examined for possible anaesthesia potential. Further, of the few olefins shown to have high inhalation toxicity and that were also introduced in other ways, the toxicity was high for intravenous injection and also high for oral administration if in lipophilic solutions[1]. It seems that there is no reason to expect that olefin hydrolysis is the sole cause of toxicity, although its enhancement of the overall effect can be substantial.

A striking correlation apparently exists between fluoro-olefins and their toxicological properties which has not been previously realized: the toxicity of a halogenated olefin is directly proportional to the reactivity of that olefin to nucleophiles.

We shall not discuss in detail the postulates of nucleophilic substitution at unsaturated fluorocarbons or of fluorcarbanion theory. Nevertheless, fluorinated olefins are rather reactive towards nucleophilic reagents to yield mostly substituted products and, more rarely, addition products. One may suggest a carbanion intermediate for these reactions although its descrite existence in some instances is not beyond question. This carbanion concept is useful as a predictor of both reactivity and products[6]. Generally, a fluorine moiety activates a double bond towards nucleophilic attack and the order of reactivity increases with intermediate carbanion stability, that is, 3° > 2° > 1°. For example, we find the following order of nucleophilic susceptibility for perfluorinated olefins:

$$(CF_3)_2C=CF_2 > CF_3CF=CF_2 > CF_2=CF_2$$

This ranking is identical to that of the comparative toxicities of these olefins.

Other halogen substituents affect olefin reactivity, usually enhancing it, although there is little information on the comparative kinetics of various fluorinated olefins towards nucleophiles. Most observations of relative nucleophilic susceptibility are deduced from the severity of experimental conditions needed to prepare vinyl ethers by reaction of olefins with alkoxides or alcohols.

In at least one instance, the relative reactivity of a *cis* : *trans* isomer pair was determined. Park and Cook[7] found that for the reaction of *cis* and *trans*-2,3-dichlorohexafluorobutene-2 with methoxide ion at 25° C, the *trans* isomer was nearly four times as reactive as the *cis* isomer. Raventos and Lemon[5]

have found that the *trans* isomer of this olefin is about three times as toxic as the *cis* isomer.

Surely these are more than coincidental relationships. Alkylating agents—compounds sensitive to nucleophiles—are a well known class of compounds possessing high biological activity[8]. That fluorinated olefins may also be alkylating agents in biological systems must also be considered. Further, it is possible that this is the principal reason for the high toxicity found in many members of this class. Of course, halide hydrolysis is a concurrent toxic mechanism and is doubtlessly responsible for lung oedema and associated disorders. We feel, however, that this hydrolysis is obscuring what is likely to be the principal toxic mode of activity of these compounds. The warning is clear: whenever one works with a polyfluorinated olefin of high nucleophilic susceptibility, and in the absence of specific toxicological information, extraordinary safety precautions are indicated.

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Chlorinated Hydrocarbon Pesticides and Related Compounds in Adipose Tissue from People of Japan

HERE we report preliminary results on the presence of hexachlorobenzene (HCB) and polychlorinated biphenyls (PCBs) in addition to dichlorodiphenyl trichloroethane (DDT), dieldrin (HEOD), heptachlor epoxide (HE) and the three isomers of hexachlorocyclohexane (α,γ,β-HCCH) in Japanese autopsy adipose tissue. A total of 241 samples were taken at the Aichi Cancer Center Research Institute, Chikusa-Ka Nagoya, Japan.

The fat samples analysed averaged 1.1 g wet weight. The procedure of Mills[1] was essentially followed for extraction and clean-up, and analysis was completed using a Micro Tek MT-220 and a Varian 2100 gas chromatograph equipped with electron capture detectors, ^{3}H or ^{63}Ni. Columns used: (1) 1.5% OV-17/1.95% OF-1 on 'Supelcoport' 80/100 and (2) 5% OV-210 on 'Supelcoport' 80/100, and maintained at temperatures of 200° C and 188° C, respectively. The injection ports were at 250° C, the ^{3}H detector at 200° C, and the ^{63}Ni detector at 315° C. Aliquots of sample extracts were compared qualitatively and quantitatively with a standard chlorinated hydrocarbon mixture (Fig. 1).
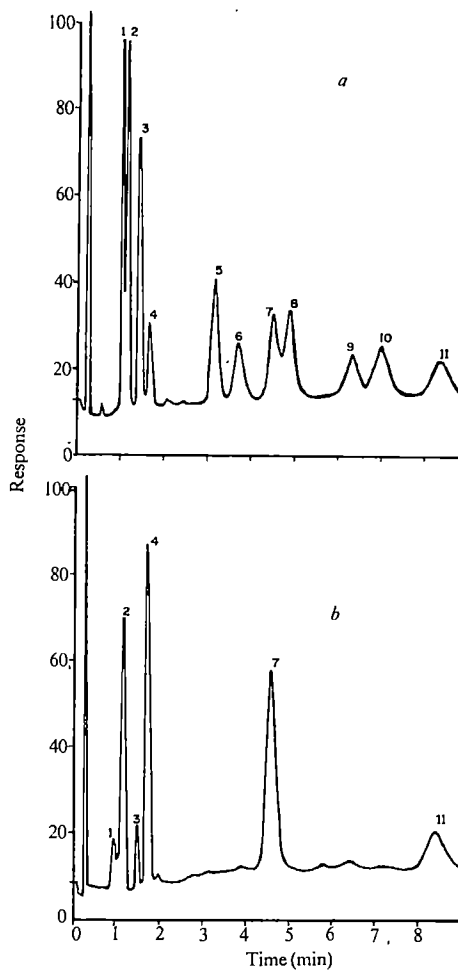
Fig. 1 Gas chromatographic traces of (*a*), standard chlorinated hydrocarbon mixture; 53 pg each of: 1, hexachlorobenzene; 2, α-HCCH; 3, γ-HCCH; 4, β-HCCH; 5, heptachlor epoxide; 6, *o,p'*-DDE; 7, *p,p'*-DDE; 8, dieldrin; 9, *o,p'*-DDT; 10, *p,p'*-DDD; and 11, *p,p'*-DDT; and (*b*), Japanese adipose tissue, 0.053 mg. Column, 6 foot × 1/8 inch glass packed with 1.5% OV-17/1.95% OF-1 on 80/100 'Supelcoport'.

As PCBs have been reported in human tissue[2,3] it was decided to analyse twenty-five samples at random for possible residue levels of PCBs by electron-capture gas-liquid chromatography following liquid-solid chromatography of the 6% fraction from 'Florisil'. To separate DDT-like materials from the PCBs, twenty samples were analysed by the procedure of Armour and Burke[4] and five samples by the procedure of Snyder and Reinert[5]. The compound *p,p'*-DDE was not completely resolved as were the other pesticides evident during electron-capture gas-liquid chromatography.

In our experience of residue tissue analysis of polychlorinated biphenyls, stored PCBs elute in the 6% fraction from 'Florisil' and after β-HCCH by gas chromatography on the two columns used in this study. Consequently, pesticide values that would not be questionable because of possible PCB contamination are HCB, α, γ and β-HCCH and dieldrin. To determine the validity of the other pesticide values reported, a comparison of pesticide concentrations before and after separation of PCB was made for the DDT-related compounds and heptachlor epoxide. This was done by comparing the residue levels found in the 6% fraction from 'Florisil' with those found in the second fraction of the PCB-separation procedures.

Two-column gas chromatography, Coulson conductometry and 'Florisil' elution patterns were accepted as sufficient confirmation for the presence of all reported compounds except hexachlorobenzene and PCBs. To substantiate the presence of HCB, one hundred samples were chosen at random and eluted with hexane through Woelm silica gel. After silica gel was
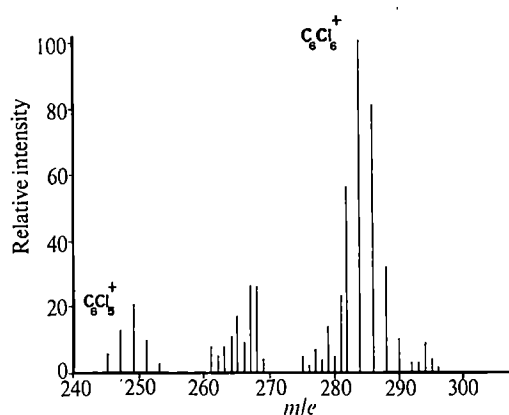
Fig. 2 Partial mass spectrum of hexachlorobenzene in composite Japanese fat. Mass spectroscopy of the composite samples for HCB and PCBs was completed under the following conditions: Instrument, LKB 9000 GC–MS equipped with a mass marker (± 0.3 mass unit); GC column temperature, 209° C; flash heater temperature, 235° C; glass coiled column, 10 foot $\times$ 1/4 inch 1.5% OV–17/1.95% OF–1 on 60/80 mesh 'Chromosorb W', H.P., A.W., DMCS: carrier gas, helium (Prep.); carrier gas pressure, 12 pound inch^{-2}; carrier gas flow rate (rotameter setting, 3), 45 cm^{3}min^{-1}; separator temperature, 225° C; source temperature, 290° C; source energy, 70 eV; accelerating voltage, 3.5 kV; trap current, 60 μA; box current, 50 μA; and leak current, 8 μA. (The chlorine isotopic pattern for Cl$_5$ is slightly distorted due, probably, to impurities.)

deactivated 5% w/v with distilled water, 1.0 g $+$ 0.01 g was added to a 5.75 inch disposable pipette plugged with silanized glass-wool. The column was pre-rinsed with 10 ml. of hexane, and each sample added in a volume of 0.5 ml. It was previously determined that HCB at a concentration of 0.1 p.p.m. eluted quantitatively in 3 ml. hexane.

The eluates were combined, evaporated and analysed by electron-capture and electrolytic conductometric detectors using column 1. Each mode showed three peaks with relative retention times to p,p'-DDE of 0.10, 0.19, 0.28 and 0.10, 0.14, 0.22, respectively. Hexachlorobenzene has relative retention times to p,p'-DDE of 0.19 and 0.22, respectively.

The composite was pipetted on preparative silica gel (F-254, 2 mm) and codeveloped with an HCB standard for 1 h in a solvent system of petroleum ether, ethyl ether and acetic acid $(90+10+1)$[6]. Under ultraviolet light (short wave) the quenching of the HCB standard and the composite were observed at an R_F of 0.62 and 0.68, respectively. The composite spot was scraped and extracted with hexane, and after evaporation of the extract to 1 ml. the composite and an HCB standard were used to determine and compare p-values[7]. The distribution of HCB between equal volumes of hexane and acetonitrile was 0.88 hexane and 0.12 acetonitrile at 25° C. The composite sample had a distribution of 0.86 hexane and 0.14 acetonitrile. These values compare favourably with previously reported data[8]. After p-value determination, the composite sample was analysed by mass spectrometry–gas chromatography.

Table 1 Concentration of Chlorinated Insecticides in 241 Japanese Fat Samples Measured by Electron-Capture Gas-Liquid Chromatography *

Pesticide	Range	Mean	Standard error ($\pm$)
α-HCCH	<0.003–10.4	0.14	0.04
β-HCCH	<0.007– 8.4	1.28	0.08
γ-HCCH	<0.003– 5.2	0.12	0.02
o,p'-DDE	<0.01 – 0.29	0.03	0.002
p,p'-DDE	<0.01 –16.5	1.78	0.13
o,p'-DDT	<0.01 – 1.12	0.08	0.006
p,p'-DDT	<0.01 – 3.09	0.54	0.03
p,p'-DDD	<0.01 – 0.58	0.04	0.004
HE	<0.01 – 0.2	0.02	0.002
HEOD	<0.01 – 0.98	0.13	0.01
HCB	<0.003– 0.77	0.08	0.006

* In p.p.m.

As the apparent presence of PCB would affect the pesticide levels, it was felt that their presence should be confirmed. A composite sample of PCB fractions was analysed by electrolytic conductivity. It was found that p,p'-DDE was not completely resolved from PCB. Following gas chromatography the composite sample was streaked on preparative silica gel (F-254, 2 mm) and codeveloped for 1 h with 'Aroclor 1254' in hexane: methylene chloride, 80 : 20 (ref. 9). 'Aroclor 1254' has an R_F value of 0.38. A corresponding area of the sample was scraped, extracted, streaked again on preparative silica gel and codeveloped in the solvent system: petroleum ether, diethyl ether and acetic acid $(90+10+1)$ with 'Aroclor 1254' for 1 h. In this system 'Aroclor 1254' had an R_F of 0.52 and the composite was 0.57. The composite spot was scraped, extracted with hexane and analysed by gas chromatography–mass spectrometry.

The initial data resulting from the usual method for the determination of chlorinated hydrocarbons are summarized in Table 1. The levels of the more common chlorinated hydrocarbons, DDT, dieldrin and heptachlor epoxide were within the range found in the United States[10]. The levels for three of the hexachlorocyclohexane isomers were quite high, particularly β-HCCH, when compared to American levels[10]. Japanese researchers[11,12] have found generally high levels of the hexachlorocyclohexanes in food and water which could explain the high levels found in the human samples. Traces of the fungicide hexachlorobenzene were also detected.

All samples analysed were positive for PCBs (Table 2). Eighty per cent of the samples had a PCB concentration of less than 1.0 p.p.m.

A comparison of pesticide concentrations, before and after the separation of PCBs for the DDT-like materials, shows that the average percentage of the initial GC response confirmed to be pesticide was HE (62), o,p'-DDE (71), p,p'-DDE (83), o,p'-DDT (50), p,p'-DDD (64), and p,p'-DDT (85). It seems, for this small sample group, that when PCBs are present they influence the pesticide values of o,p'-DDT, HE, p,p'-DDD, o,p'-DDE more so than p,p'-DDE and p,p'-DDT.

The normalized mass spectrum of the composite sample
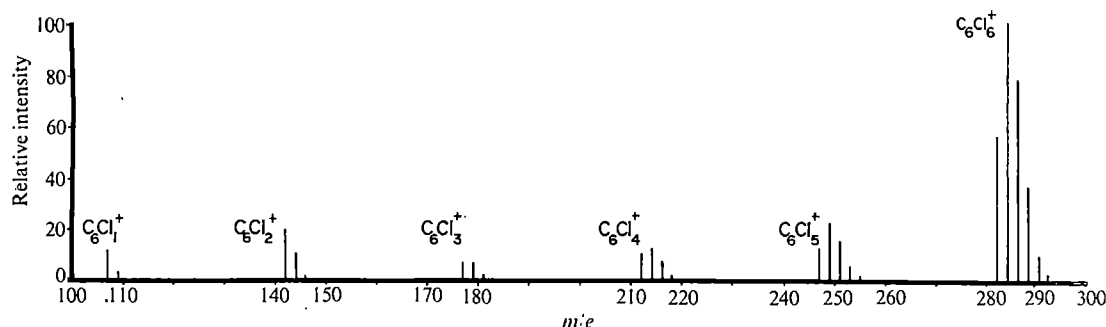
Fig. 3 Mass spectrum of hexachlorobenzene depicting successive loss of chlorine from the parent ion.
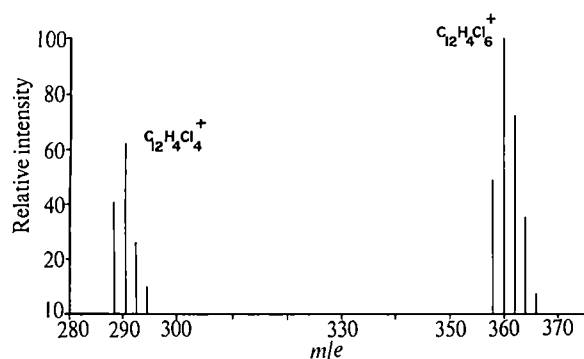
Fig. 4 Partical mass spectrum of hexachlorobiphenyl (PCB) in composite Japanese fat.

analysed for HCB is shown in Fig. 2. The mass spectrum indicates a molecular ion at $m/e = 282$. A chlorine isotopic cluster of six chlorine atoms was observed and indicated that an empirical formula for this ion cluster would be C_6Cl_6. Further examination of the mass spectrum reveals only one major fragment at $m/e = 247$, containing a chlorine isotopic cluster of five chlorine atoms indicating the loss of one Cl atom from the parent ion.

Mass spectral examination of an HCB standard (Fig. 3) shows the molecular ion at $m/e = 282$ and fragments at $m/e = 247$, 212, 177, 142 and 107 with isotopic clusters indicative of five, four, three, two and one chlorine atoms, respectively. The absence of the ion fragments in the low mass range of the spectrum of the composite sample resulted from, first, a low sample enrichment in the analyser tube; and second, the presence of more abundant ions contributed by compounds of high carbon content, similar to fats.

The spectrum contains the expected substituted benzene fragmentation pattern. The parent ion and subsequent ion fragment support the gas chromatography, liquid-solid chromatography, thin layer chromatography and p-value data indicating the presence of HCB in the composite samples. The normalized mass spectrum of the composite sample analysed for hexachlorobiphenyl is shown in Fig. 4. This composite sample was found to contain p,p'-DDE, which was evident at an earlier stage of analysis. Although earlier analysis showed the presence of several PCB-type constituents, only one was of sufficient concentration for mass spectral confirmation. The molecular ion at $m/e = 358$ with a chlorine isotopic cluster of 6 is the hexachlorobiphenyl with a fragment at $m/e = 288$ containing four chlorine atoms. The loss of chlorine atoms in pairs from the parent ion has been the PCB fragmentation pattern observed in this laboratory.

The presence of a fungicide HCB, a chlorinated biphenyl and normally occurring pesticides has been confirmed in human adipose tissue from Japan. The contribution that the presence of PCB has on the reported storage values of the more commonly occurring pesticides has been shown. The levels of HCCHs, PCBs and DDT are slightly lower but of the same

Table 2 Concentration of Polychlorinated Biphenyls in Japanese Fat*

Number of samples analysed	Range	Mean§	Standard error (±)
5†	0.45–0.56	0.51	±0.017
20‡	0.30–1.48	0.80	±0.065

* In p.p.m.
† PCBs separated by method of Snyder and Reinert, AR 1254 at 0.5 p.p.m. gave 62% recovery in fraction I ($N=3$).
‡ PCBs separated by method of Armour and Burke, AR 1254 at 0.5 p.p.m. gave 87% recovery in fraction I ($N=3$).
§ These values are based on total area under the curve using 'Aroclor 1254' as a reference standard and are exclusive of sample responses with the same retention time as $p,p,'$DDE, no correction was made for standard recovery.

order of magnitude as those reported by Nishimoto et al.[13]. HCB was not reported by these workers.

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Use of "Whole Egg Residues" in Pesticide/Eggshell Studies

HAZELTINE[1] questions the well established belief that DDE probably causes eggshell thinning in brown pelicans chiefly by finding four points of disagreement with the proposal by Blus et al.[2] that a concentration-effect relationship seems to exist between DDE in eggs and shell thickness. In their subsequent reply, Blus et al.[3] refute Hazeltine's criticisms. There is a further argument against Hazeltine's third criticism of Blus et al.'s conclusions; and the argument has an important bearing on the interpretation of analyses based on "whole egg residues".

Hazeltine expresses the view that the "whole egg residues" are valueless in pesticide/eggshell studies of incubated eggs on the basis of his assumption that the residues are metabolized during incubation. He provides no data for residues expressed on a whole egg (fresh weight) basis, and gives no acceptable evidence to show that DDE or other residues are metabolized (that is, broken down chemically), as distinct from mobilized. Even if we accept that the residues are indeed metabolized during incubation, this does not necessarily make the use of the whole egg residues inappropriate. If DDE residues are metabolized during incubation, then the whole egg residues for incubated eggs will tend to be low. Bearing in mind the thinning of eggshells by withdrawal of calcium in embryonic development during incubation, it is obvious that in the presence of DDE metabolism during incubation, the use of the whole egg

residues for pesticide/eggshell studies would provide a conservative test if the correlation between the eggshell thickness and the levels of residue is asserted to be negative. Blus et al.'s "highly significant regression ($P < 0.01$)" with a negative slope is then likely to be even more significant than suggested by the probability value quoted.

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DDE in Eggs and Embryos of Brown Pelicans

HAZELTINE[1] claims to have demonstrated that DDE residues are metabolized by developing embryos of brown pelicans (*Pelecanus occidentalis*). This conflicts with experimental work[2] on Japanese quail (*Coturnix coturnix*), in which incubation did not seem to affect total residue levels in eggs, except for some conversion of p,p'-DDT to p,p'-DDE.

Hazeltine's claim seems to be based on a comparison of DDE levels in the yolks of four incubated and five fresh eggs. As he made clear in the text, the column labelled "Weight yolk" in his Table 1 actually refers to the yolk plus embryo. The apparent 3.2-fold decrease in the mean concentration of DDE in "yolk" simply reflects the 2.6-fold increase in the weight of the yolk+embryo, as the embryos absorbed material from the white. In Hazeltine's sample the whole-egg residues of DDE were slightly smaller in the incubated eggs (mean 2.53 mg) than in the fresh eggs (3.62 mg), but the difference is not statistically significant and in any case this does not demonstrate metabolism of DDE. It is more simply explained by the fact that eggs with higher levels of DDE are broken more frequently during incubation, so that they are less frequently available for collection: this differential breakage has been demonstrated not only in the brown pelican[3], but also in other species[4-7]. For the same reason[3-7] samples of incubated eggs are expected to have thicker shells, on the average, than fresh eggs, as in Hazeltine's sample (means 0.390 mm and 0.372 mm, respectively).

Hazeltine also reported that eggshell thickness was positively correlated with DDE concentration in the lipids of the "yolk". But the latter is not an appropriate measure of the DDE levels in the eggs, because it increases during incubation as the egg lipids are reduced by metabolism[8] (from 3.80 g to 2.26 g in Hazeltine's sample). The most appropriate measures are the whole-egg residue or whole-egg concentration, which reflect the levels of DDE circulating in the female at the time of laying[9-11]. In Hazeltine's sample, the Spearman rank correlation coefficient r_s between whole-egg residue of DDE and eggshell thickness is $+0.244$ (not $+0.477$ as stated in Hazeltine's Table 2). This is not statistically significant, which is not surprising in a small sample with a very small range in eggshell thickness: but the points fall close to the regression lines of Risebrough[12] and Blus et al.[13]. As Hazeltine points out (his Table 3), in Risebrough's larger sample the correlation is negative and highly significant ($r_s = -0.4318$, $P < 0.01$).

Hazeltine also stated that non-parametric statistics should have been used by Blus et al.[13] to test the relationship between eggshell thickness and DDE residues, because these variables were "not bi-variantly normally distributed". This would be valid if the goal of the study had been simply to demonstrate

association of eggshell thinning with DDE, but Blus et al.[13] were attempting to define the dose-response relation. Parametric regression techniques require only that the dependent variable be random and normally distributed about the regression line[14]. This condition was satisfied by the brown pelican eggshell data of both Risebrough[12] and Blus et al.[13], and both found a good fit to a logarithmic dose-response relation. A logarithmic relation between eggshell thickness and DDE residues in eggs has also been reported in wild peregrine falcons (*Falco peregrinus*)[4,15] and in experimental mallards (*Anas platyrhynchos*)[16]. The advantage of applying a logarithmic transformation to the DDE variable is that it is then possible to use multiple linear regression techniques to separate the effects of co-existing pollutants. This was done by both Blus et al.[17,18] and Risebrough[12], who found independently that most of the variance in eggshell thickness was explained by the log DDE and DDE variables, and no significant fraction by any other chemicals.

Hazeltine also criticized Blus et al. for combining data from brown pelicans of two different subspecies. Blus et al. corrected for the known difference between the subspecies by using as dependent variable the eggshell thickness expressed as a percentage of the pre-1947 mean for the subspecies. In any case this criticism cannot be applied to Risebrough's data, which were all drawn from Pacific Coast populations[12].

The association of eggshell thinning in birds with p,p'-DDE is one of the best known of all environmental phenomena[19]. It has been shown so many times in both wild and captive species[3-7,12,13,16-18] that at least one journal has complained about receiving further "verifications of phenomena already fully demonstrated"[20]. Scientific work in this area is now devoted to elucidating details such as the form of the dose-response relation and the reasons for the known interspecific differences in sensitivity. The brown pelican is one of the species in which the phenomenon has been explored most fully[3,12,13,17,18,21,22]. It is therefore somewhat odd to find another letter[1] discussing whether the association exists, based on a sample too small and homogeneous to demonstrate anything. In fact, Hazeltine's nine eggs fall exactly into the pattern of eggshell thinning known from previous work[12,13,22], and his data add nothing to previous knowledge except for his demonstration that "yolks" grow larger during incubation.

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Inhibition of Lectins by Antifreeze Glycoproteins from an Antarctic Fish

CERTAIN Antarctic fishes can resist freezing, even at ambient water temperatures as low as $-1.9°$ C, partly because of the presence in their serum of a unique group of "antifreeze" glycoproteins[1-5]. These glycoproteins are composed of repeating units of the triglycopeptide, Ala-Ala-Thr-O-disaccharide. The disaccharide is galactosyl-N-acetylgalactosamine, with internal linkage β, $1\rightarrow3$ (ref. 6) or β, $1\rightarrow4$ (ref. 7). Three active glycoproteins differing only in polymer length have been characterized with molecular weights of approximately 11,000, 17,000, and 22,000. In addition to these active glycoproteins, two smaller related glycoproteins have been found. These differ from the large active glycoproteins by their comparative inactivity in depressing the freezing point, their smaller molecular weights (approximately 2,500 and 4,500), and the substitution of a proline for some of the alanines following threonine[8,9].

We initiated immunological studies in an attempt to develop sensitive methods for studying these glycoproteins. Both the active and inactive glycoproteins failed to precipitate with horse antipneumococcal type IV or type XIV sera (unpublished observations of M. J. Heidelberger, jun.). At Heidelberger's suggestion we made tests for inhibition of the haemagglutination by plant lectins. In this way we have demonstrated a distinct difference between these active and inactive antifreeze fish glycoproteins.

The active and inactive antifreeze glycoproteins were prepared from the blood serum of specimens of the fish *Trematomus borchgrevinki*, caught in Antarctica. The blood was centrifuged after it had clotted; the clear serum was frozen for transport to the University of California, Davis. Purification of the active and inactive antifreeze glycoproteins was as previously described[1]. The active antifreeze was a mixture of fractions one to five and the inactive fractions were mixtures of seven and eight[1].

Lectins were prepared from slurries of finely ground seeds made up (20% w/v) in 0.15 M NaCl, extracted overnight at $4°$ C and cleared of insoluble materials by coarse filtration through surgical gauze and centrifugation at 10,000*g* for 10 min. Considerable inactive coagulum was removed by subjecting the clarified extracts to $65°$ C for 20 min followed by recentrifugation. Sodium azide (0.1%) was added as a preservative and the lectin preparations were then stored at $4°$ C without notable loss of activity.

To study the effects of holding live *T. borchgrevinki* at a temperature above the freezing point, approximately 30 fish were placed in temperature-controlled tanks in the biolaboratory at McMurdo Station, Antarctica. The temperature of these tanks was maintained at $3\pm1°$ C. Fish were taken and bled at weekly intervals until termination of the experiment at 5 weeks. The blood was handled as above.

Samples of mammalian saliva from both "secretor" and "non-secretor" individuals were prepared as previously described[10]. All sugars were of reagent grade; α- and β-lactose preparations were provided by J. R. Spies.

Small molecular weight glycopeptides were prepared from active antifreeze as previously described[3]. Mixtures of small glycopeptides (mainly di- to hexa-glycopeptides) were separated from the digest by electrophoresis.

Other samples of blood plasma or serum were obtained by centrifugation of the clotted or unclotted blood from human donors in the laboratory, from salmon (*Oncorhynchus tschawtscha*) (obtained from the California Fish and Game Division) or from rabbits (obtained from the animal colony at Davis). Blood cells of diverse origin were available from regular laboratory stocks or from the School of Veterinary Medicine at Davis. Haemagglutination tests and sugar inhibition studies were carried out as previously described[10,11].

In Table 1 we show the potency with which the antifreeze-active glycoprotein inhibited haemagglutination by Osage-orange (*Maclura pomifera*) lectin. At a final concentration in the reaction mixtures of less than 1 μg ml.$^{-1}$ the active antifreeze glycoprotein completely inhibited haemagglutination of both human group-O and sheep erythrocytes. By contrast, the inactive antifreeze glycoprotein was some fifty to one hundred times less active as an inhibitor. Several other randomly tested preparations containing glycoproteins of diverse origin were either inactive or comparatively weak inhibitors (Table 1).

The active antifreeze and inactive antifreeze glycoproteins tested at 100 μg ml.$^{-1}$ starting concentration also failed to inhibit numerous other lectins as well as immune animal sera possessing various haemagglutinating specificities. The striking inhibitory activity of the intact active antifreeze glycoprotein for the Osage-orange lectin was further illustrated by the finding of little or no inhibitory activities by either the blood sera of man, rabbit, and a cool-water fish, the salmon; or preparations of

Table 1 Haemagglutination Inhibitors

Agglutinating reagent	Erythrocytes tested	Saliva* Human Non-sec	Saliva* Human O sec	Rhesus Sec	Serum Fraction VI† Pig	Serum Fraction VI† Sheep	Ovomucoid‡	Antifreeze glycoprotein‡ Active	Antifreeze glycoprotein‡ Inactive
Osage-orange lectin	Human O	(2)	(16)	(64)	(32)	(4)	+++	(800)	(8)
	Rhesus	(1)	(2)	(64)	(4)	(1)	+++	(200)	(4)
	Sheep	++	(8)	(64)	(64)	(4)	+++	(600)	(8)
Ricin	Human O	++	++	(2)	(1)	+++	++	++	++
	Rhesus	+	++	(4)	(4)	+++	++	+++	+++
	Chicken	++	+++	(4)	(2)	++	+++	+++	+++

* Sec=boiled "secretor" saliva.
† Commercial glycoprotein preparations tested as inhibitors at a starting concentration of 1 mg ml.$^{-1}$.
‡ Tested at starting concentrations of 1 mg ml.$^{-1}$.
Numbers enclosed by parentheses denote reciprocal of maximum dilution of inhibitor solution which still completely inhibited macroscopic agglutination when mixed with an equal volume of 1:8-titre agglutinating reagent before the introduction of one volume of a 2% suspension of thrice saline-washed erythrocytes. Non-inhibited macroscopic agglutination graded from + to +++ following 20 to 30 min tube incubation at $22°$ and centrifugation for 15 s at 1,000*g*.

mixtures of small glycopeptides produced by elastase hydrolysis of active antifreeze glycoprotein. Also, when live specimens of *T. borchgrevinki* were kept at $3 \pm 1°$ C for periods of up to five weeks, the lectin-inhibition titres did not change. The antifreeze activities of the blood also did not appear to change significantly during this time, although fluctuations were noted.

In comparative studies of inhibition with 11 different monosaccharides, three sugars with D-galactose configuration (N-acetylgalactosamine, D-galactose, and 2-deoxy-D-galactose) and α-methyl-D-mannoside notably inhibited the Osage-orange lectin, decreasing in potency in the order indicated. No detectable inhibition was obtained with 6-deoxy-D-galactose (D-fucose), L-fucose, D-glucose, D-mannose, or 3-O-methyl-D-glucose tested at 0.5 M starting concentration.

Of four oligosaccharides with non-reducing end-groups of D-galactose (tested at a 10% (w/v) starting concentration), only melibiose and raffinose notably inhibited the Osage-orange lectin. α- and β-Lactose were both ineffectual inhibitors of the Osage-orange lectin, notwithstanding the internal β linkage in the antifreeze disaccharide moieties. Our observations, nevertheless, are largely consistent with earlier and more extensive oligosaccharide inhibition studies on the Osage-orange lectin[12-14]. In one of these[14] a disaccharide with a reported structure possibly identical with the antifreeze disaccharide (β-D-galactosyl-N-acetylgalactosamine) was less active as an inhibitor of the Osage-orange lectin than either melibiose (α-D-galactosyl-(1→6)-D-glucose) or N-acetylgalactosamine.

Notable inhibition of the Osage-orange lectin by D-galactose, N-acetylgalactosamine and 2-deoxy-D-galactose, but not by 6-deoxy-D-galactose, in turn indicates the likely participation in Osage-orange lectin interactions of hydroxyl groups at the 3, 4, and 6 carbon positions of the terminal D-galactosyl residues in the intact antifreeze-active glycoprotein. None of the *T. borchgrevinki* glycoproteins inhibited the castor-bean lectin (Ricin), which is inhibitable with either D-galactose or 6-deoxy-D-galactose and is reportedly reactive with all D-galactosyl residues possessing accessible hydroxyl groups at the 2, 3, and 4 carbon positions[15]. These observations indicate strongly that the hydroxyl groups at the 3, 4, and 6 carbon positions of the terminal D-galactosyl residues of the intact active antifreeze glycoproteins are important for the interaction with Osage-orange lectin. It seems that the polypeptide backbone or adjacent disaccharides in the repeating triglycopeptide units confer on the terminal D-galactosyl residues in the intact active antifreeze glycoprotein molecules a spatial positioning particularly favourable for interactions with the Osage-orange lectin. The only other possibility seems to be the existence of an unrecognized structure which is hydrolysed by the elastase.

The quantities of freezing-point depressing glycoproteins required for the inhibition of the lectin and depression of the freezing point are <0.1 μg and >1.0 mg, respectively; that is, the lectin assay is $>10^4$ times more sensitive. The lectin assay therefore provides a micro method for determining the amounts of the glycoprotein in tissues and fluids of polar fishes and for studying its biosynthesis and metabolism.

Both the activity for inhibiting the lectin and the activity for depressing the freezing point seem to be dependent upon the primary structure of the glycoproteins with regular spacings of the disaccharides along the peptide chain. This has been shown for both processes by the very low activities of the glycopeptides obtained by proteolysis from the active freezing point-depressing glycoproteins and the very low activity of the smaller molecular weight inactive freezing point-depressing glycoproteins. Other studies have shown that oxidation of C-6 alcohol groups of the galactose residues to carboxyl groups destroys activity for inhibiting the lectin as well as for depressing the freezing point[6,7]. Further studies on relating structural requirements for these two different activities are under way[16].

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Are Mosquitoes Monogamous?

CONFUSION has arisen within the past 5 years with regard to two related aspects of the most basic feature of the sexual behaviour of mosquitoes. The first aspect concerns the definition and use of the word, *monogamous*. In various studies on the biology of reproduction in mosquitoes, Craig and his associates[1-3] refer to "monogamous" female mosquitoes using it to refer to one sex exclusive of the other, as if the term were derived from the word gamete and could be used to refer to a female mosquito that had received the spermatozoa from only one male. The word monogamous is in fact derived from a Greek word γαμος (gamous) meaning marriage[4], and, since 1758 the zoological definition has been "the habit of living in pairs, or having only one mate"[4]. The word gamete, on the other hand, is derived from a Greek word γαμετη (gameta), meaning either husband or wife[4]. The word mate is defined as an associate or companion, or one of a pair of animals. Both the Greeks and the English have separate words for sex, copulation and insemination, and a totally different word

monogamous for having only one mate. The word monogamous is complicated because it can mean having only one mate at a time or having only one mate for life. Having one mate does not necessarily mean that the individuals of one pair copulate; the word copulate means to join, couple, unite, or connect but does not specify insemination. It will be shown in the following section that Craig's use[1] of the word monogamous is peculiarly inappropriate for the mosquito *Aedes (Stegomyia) aegypti* (L.).

The second aspect of this problem concerns a seemingly simple direct observation of whether an individual female *A. aegypti* copulates more than once during her lifetime. It was originally believed that *A. aegypti* females copulate with many males under free-flying conditions in the laboratory[5]. Roth[5] observed that one male in a cage with 16 virgin females copulated 30 times in 30 min, and that 11 males copulated 50 times in 1 h with a single previously virgin female. Wheeler and Jones[6] found that male *aegypti* could be forced to copulate with some newly-emerged females but did not inseminate them. This was influenced by the secretions of the corpora allata and varied with the strain of *aegypti*[7]. Male *aegypti* could not be force-copulated with freshly inseminated females[8]. While under free-flying conditions many of the once-mated females copulated a second, although significantly shorter, time than the first[9]. While Gwadz and Craig[2] stated that *aegypti* females may copulate repeatedly, it was subsequently concluded, from observations with tethered females[3], that they copulate only once and falsely seem to copulate thereafter. Gillett[10] reported many individual and sequential (single pair) matings of *aegypti*, and that one free-flying female mated with 40 different males.

My observations were made on the Bangkok strain of *A. aegypti*. To demonstrate whether free-flying females would copulate (or seem to copulate) with only one male and with this male more than once, ten individual couples were placed in separate cages and observed under undisturbed conditions 4 h per day for 5 to 7 days. Most of the couples copulated (or seemed to do so) more than once with a given partner under these strictly monogamous conditions. The maximum number of copulations occurred on the third day of monogamous co-habitation, when the caged mosquitoes flew about more often than on other days. Over a 7-day period, four out of five couples made 75 genital contacts during 28 h of direct observation; one couple was never seen to copulate. I conclude that females will copulate repeatedly with the same male when only one is available. Females in cages with many males have also been seen to couple repeatedly with one male.

It was possible in many cases to distinguish clearly between pseudocopulations and true copulations among free-flying mosquitoes in a cage. Most pseudocopulations were very short contacts (less than 1–4 s); the males either attached their claspers to a female's cerci or else clasped her terminal sternum and in either case only lightly. Often the males made a series of rapid thrusts with their terminalia in the direction of the female's terminalium without actually clasping any structures of the female.

To determine whether females would copulate with more than one male, a female which had had 13 observed genital contacts with one male over a 6-day period was sequentially placed in a series of 5 cages, each with a different virgin male, and the cages were manually agitated periodically for 5 min to induce flight activity. While only pseudocopulations were seen with each of the first 4 males, the fifth male definitely copulated with this female and for an abnormally long time (250.7 s). After this, a series of virgin females of known ages (1 to 13 days old) were individually blown into a cage of 20 highly active males and observed for 5 min. The 52 females were continuously disturbed to fly whenever they landed, and appeared to copulate with from 1 to 12 males in 5 min with an average of about 5 males. During these tests, 2 males, were seen attempting to copulate simultaneously with one female in 14 cases, 3 males were observed trying to establish genital contact with one female at the same time in 9 cases, and more than 3

males were found trying to mate with a single female concurrently on 4 occasions. Similar activities can be observed in colony cages. In a special test, one female was observed to copulate (or pseudocopulate) with a total of 15 different males over a period of 3 days.

The duration of the first genital contact versus the longest subsequent contact was recorded for 47 couples during these studies. It was found that in 57.4% of the cases, the longest copulation was not the first one. In general, the second genital contact (when it occurred shortly after the first copulation) was significantly shorter than the first one and was often a pseudocopulation.

When virgin females were placed in cages with 5 virgin males and the cages manually shaken for 5 min, first copulations almost invariably resulted in insemination, if the individuals remained in genital contact for 6 s. It was necessary to use only virgin males in these tests because it was found that when 43 virgin females were individually blown into a cage containing 20 unchanged males, only 74% were inseminated by the first copulation.

I conclude that while *Aedes aegypti* may copulate repeatedly with only one mate over a period of days under strictly monogamous conditions, under normal laboratory conditions this species is a polygamous insect, and that the female normally copulates more than once with one or many males but usually gets inseminated only once if she is a virgin when she copulates. This is in agreement with the earlier work of Roth[5] and Gillett[10], but not with Gwadz *et al.*[3], that the female of this species copulates only once during her lifetime.

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Competitive Exclusion in Herbaceous Vegetation

IN maintaining or reconstructing types of herbaceous vegetation in which the density of flowering plants exceeds 20 species/m²—the so-called "species-rich" communities, success is often frustrated by competitive exclusion. Here I describe an attempt to identify criteria with which to assess or anticipate the effect of competitive exclusion both at individual sites and in different types of vegetation.

Herbaceous plants have been classified according to the extent to which certain competitive attributes are evident in the genotype. Four consistent features of "competitive" species may be recognized[1–14]. They are (1) tall stature; (2) a growth form (usually a large densely-branched rhizome or expanded tussock structure) which allows extensive and intensive exploitation of the environment above and below ground; (3) a high maximum potential relative growth rate,

Table 1 Examples illustrating the Derivation of the Competitive Index

Species	Attributes				Competitive index (total/2)
	a	b	c	d	
Chamaenerion angustifolium	5	5	5	2	8.5
Arrhenatherum elatius	5	4	4	3	8.0
Brachypodium pinnatum	3	4	3	5	7.5
Ranunculus repens	3	5	3	1	6.0
Helictotrichon pratense	3	2	3	2	5.0
Taraxacum officinale	3	1	4	1	4.5
Festuca ovina	2	1	3	2	4.0
Campanula rotundifolia	2	2	3	0	3.5
Arenaria serpyllifolia	1	0	4	0	2.5

a, Maximum plant height (Clapham, Tutin and Warburg[15]). 1, <26 cm; 2, 26–50 cm; 3, 51–75 cm; 4, 76–100 cm; 5, >100 cm. b, Morphology (Clapham, Tutin and Warburg and personal observations). 0, Small therophytes; 1, robust therophytes; 2, perennials with compact unbranched rhizome or forming small (<10 cm diameter) tussock; 3, perennials with rhizomatous system or tussock attaining diameter 10–25 cm; 4, perennials attaining diameter 26–100 cm; 5, perennials attaining diameter >100 cm. c, Maximum potential relative growth rate (Grime and Hunt, unpublished). 1, RGR_{max} <2.1 mg g^{-1} h^{-1}; 2, 2.1–4.0 mg g^{-1} h^{-1}; 3, 4.1–6.0 mg g^{-1} h^{-1}; 4, 6.1–8.0 mg g^{-1} h^{-1}; 5, >8.0 mg g^{-1} h^{-1}. Where no estimate is available a provisional score of 3 has been used. d, Maximum accumulation of persistent (from one growing season to the next) litter produced by the species (personal observations). 0, None; 1, thin discontinuous cover; 2, thin continuous cover; 3, up to 1 cm depth; 4, up to 5 cm depth; 5, >5 cm depth.

and (4) a tendency to deposit a dense layer of litter on the ground surface. It is practicable to score plant species with respect to each of these features and to use the sum of the scores to provide a competitive index (CI) over a scale of 0–10 (Table 1).
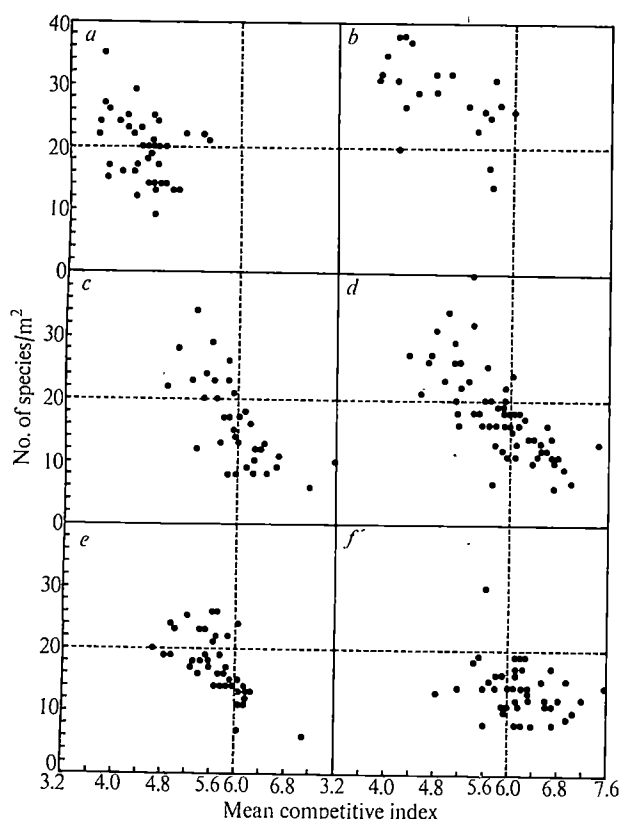
Fig. 1 Relationship between "mean competitive index" and species density in six habitats sampled widely from the same geographical area (Grime and Hodgson, unpublished). a, Limestone outcrops with discontinuous soil cover; b, unenclosed limestone pastures; c, enclosed pastures; d, derelict limestone grassland; e, meadows; f, road verges. The contribution of each species to the mean competitive index is weighted in proportion to its frequency in the m^2 sample of vegetation.
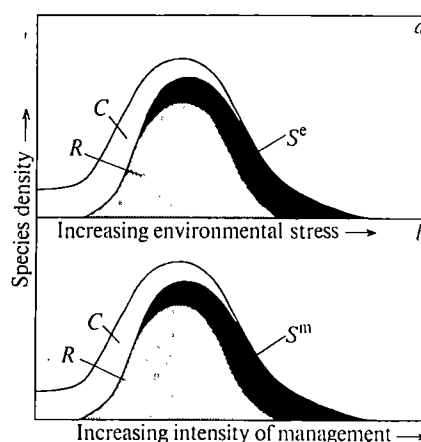
Fig. 2 Diagrams representing impact upon species density of (a) intensity of environmental stress and (b) intensity of grazing, mowing, etc. C, Species of high competitive index. $S^e, S^{g, m, b, t}$, Species (or ecotypes) of high resistance to the prevailing stresses imposed by environment or by grazing, mowing, burning or trampling respectively. R, Remaining species.

As it has been calculated in this paper, the CI incorporates a subjective component, fails to take account of ecotypic variation and ignores certain competitive attributes such as the release of phytotoxic compounds. Despite this lack of refinement, however, the index appears to be informative.

In Fig. 1 the CI has been used to assess the importance of competitive exclusion in the control of species density in six types of vegetation sampled from the same geographical area. For each square metre sample of vegetation a mean value calculated from the competitive indices of the component species has been plotted against species density. The data confirm that where species of high CI are prominent (that is mean CI>6.0) species densities are consistently low (<20 species m^{-2}). The results indicate a low incidence of competitive exclusion on limestone outcrops and in limestone pastures. In contrast, there is strong evidence that competition is a causal factor in the maintenance of the rather low species densities encountered in the samples from road verges. In the three remaining types (enclosed pastures, derelict limestone grassland and meadows) species density varies widely but in each there is a marked decline with increasing mean CI.

On the basis of previous studies[7,11,14,16–29] and the results of this investigation, I suggest that two mechanisms may bring about the low incidence of species of high CI in vegetation of high species density. One is the result of environmental stress induced by factors such as drought and mineral nutrient deficiencies, and the other is brought about by phenomena such as grazing, mowing, burning and trampling, which by defoliation or by causing other forms of damage to the vegetation tend to prevent potentially competitive species from attaining maximum size and vigour and reduce litter accumulation.

A parallel exists, therefore, between the influence of increasing environmental stress and that of increasing damage intensity, by grazing or mowing for example, on species density. According to the model proposed in Fig. 2a, under conditions of low environmental stress productivity is high and species of high CI attain maximum vigour and species density is low owing to competitive exclusion. Under conditions of increased environmental stress, the competitive species decline in vigour and species of lower competitive ability are able to survive. With further reductions in productivity species density falls as conditions of extreme environmental stress are reached and species density is limited by the scarcity of species tolerant of the specific conditions limiting productivity. This model is consistent with the observation of Odum[30] that "the greatest diversity occurs in the moderate or middle range of a physical
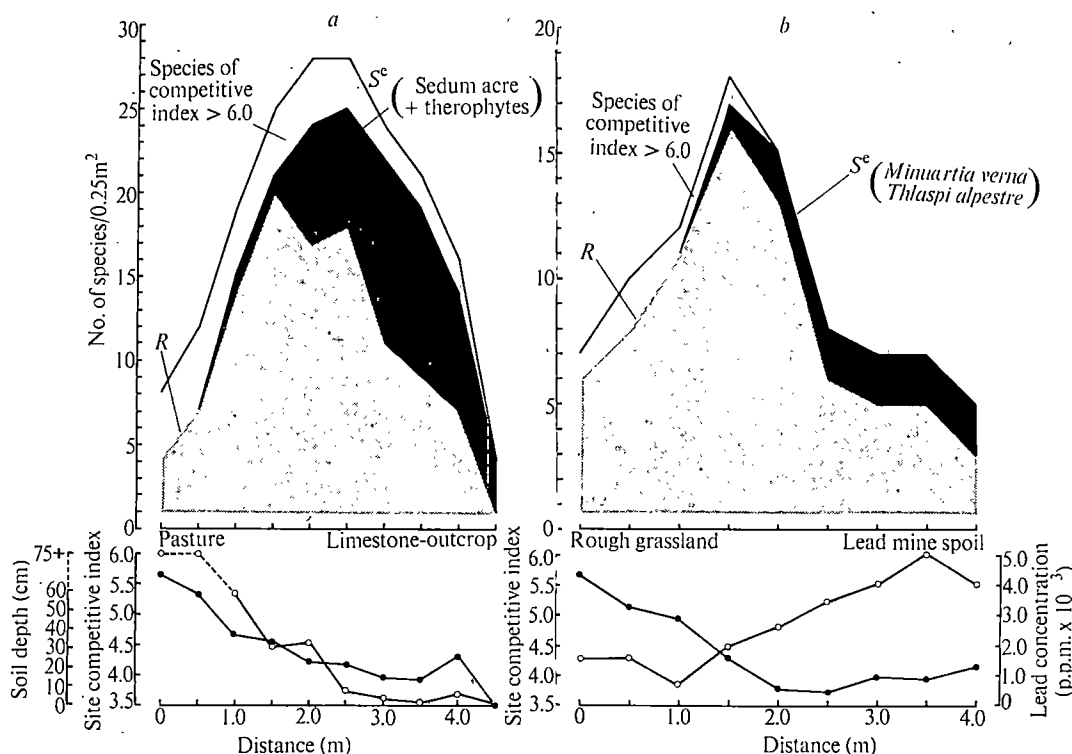
Fig. 3 Transects along natural gradients of increasing environmental stress. *a*, Boundary between rough pasture and a limestone outcrop (Coombsdale, Derbyshire). *b*, Margin of a spoil heap at a derelict lead mine (Winster, Derbyshire). Lead was extracted from the surface soil (0–3 cm) using normal ammonium acetate adjusted to *p*H 3.0. Shading and symbols as in Fig. 2.

gradient." Data conforming to the model have been obtained from transects along naturally-occurring gradients in environmental stress (Fig. 3).

With respect to the gradient of increasing intensity of grazing, mowing, etc. (Fig. 2*b*), the pattern is essentially similar. Assuming that productivity is sufficiently high, competitive exclusion will occur at low intensity of defoliation and damage. At higher intensities, species of high CI are suppressed and conditions favourable to less aggressive species occur. At the highest intensities species density would be expected to fall as a situation is reached in which only a small number of species are tolerant of the specific form of damage sustained. It is difficult to find situations in the field which illustrate all features of the latter model. Gradients in intensity of factors such as grazing, mowing and burning rarely extend over the full range represented in Fig. 2*b*. A possible exception to this arises in conditions of excessive trampling (Fig. 4) although here it is recognized that effects such as soil compaction may be involved, causing environmental stress.

From a practical standpoint, therefore, there is a need to determine the relative importance of such extrinsic factors in maintaining high species density at particular sites. A possible solution to this problem is to recognize the inverse relationship between net environmental stress and productivity and to use the maximum potential relative growth rates (RGR_{max}) of the perennial species present at each site to derive an index of the latter. A correlation between RGR_{max} and site productivity may be inferred from a number of studies[19,31-34] and comparisons such as that illustrated in Fig. 5 confirm that there is a consistent difference between productive and unproductive vegetation with respect to the potential growth rates of the component perennial species.

An index based upon RGR_{max} would appear to be promising not only in field assessments of the intensity of grazing, mowing, burning or trampling necessary to initiate or maintain high species density but also as a guide to the

stability of herbaceous vegetation. It is to be expected that vegetation composed of species with high potential growth rates (especially where some are suppressed specimens of species of High CI (Fig. 5*a*)) will show a rapid decline in
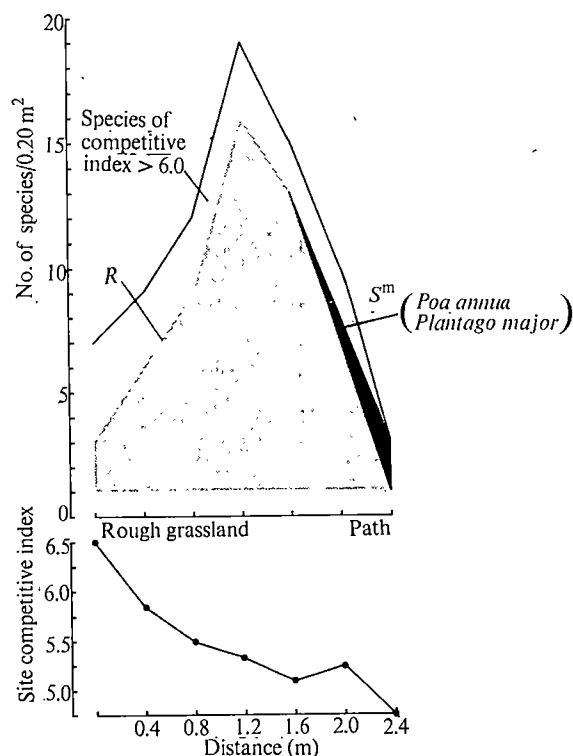
Fig. 4 Transect across the margin of a path through rough grassland (Maltby Low Common Nature Reserve, Yorkshire). Shading and symbols as in Fig. 2.
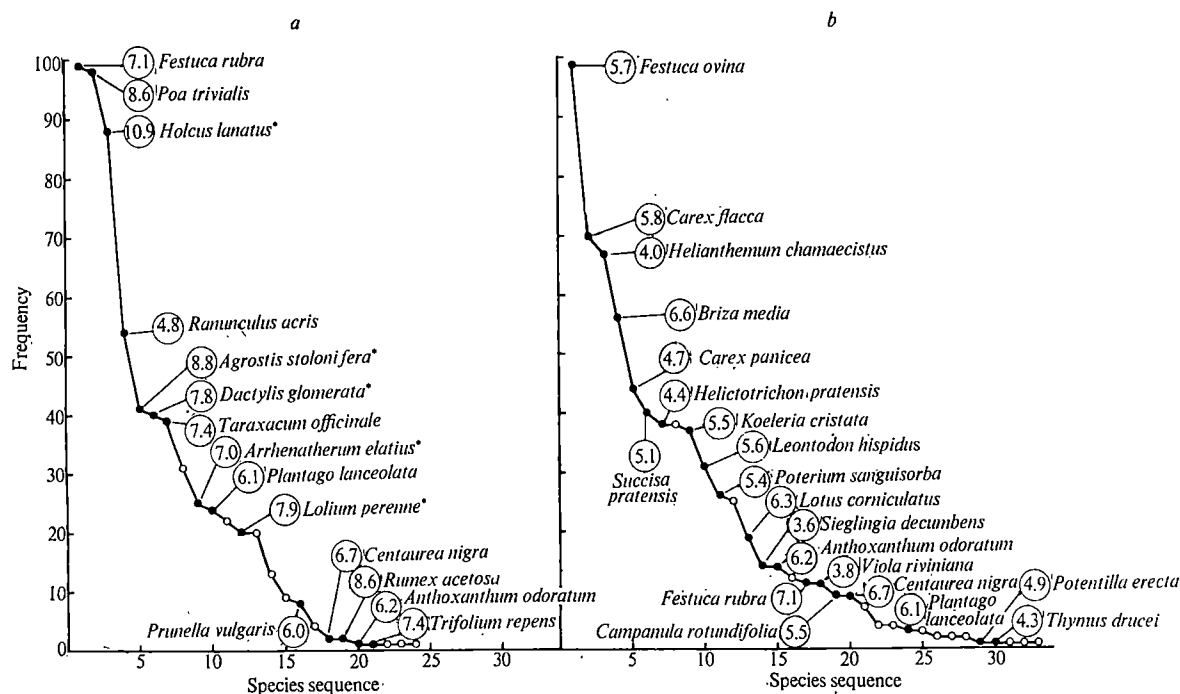
Fig. 5 Comparison of two m² samples of species-rich vegetation with respect to the potential growth rates of the component species. *a*, Productive meadow (Coombsdale, Derbyshire). *b*, Ancient limestone pasture (Cressbrookdale, Derbyshire). (Grime and Hunt, unpublished.) In each figure the species are arranged in order of decreasing % occurrence in 10×10 cm subdivisions of the m² quadrat. The encircled values refer to the RGR_{max} of the species. The open circles indicate species for which no growth-rate estimations are available. * Species of high (> 6.0) competitive index.

species density when grazing or mowing is relaxed. Where values for RGR_{max} are low the ensuing reduction in species density is likely to proceed at a relatively slow rate.

Here differences in species density have been related to variation in stress imposed by environment or by certain forms of management and to variation in the frequency and vigour of species of high competitive ability. The impact of additional factors such as site accessibility and degree of niche-differentiation upon species density will be reported elsewhere.

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Gestation Period for Australopithecus

LEUTENEGGER[1] has provided estimates of the foetal size at birth of two species of *Australopithecus*. Huggett and Widdas[2] drew attention to the relationship between foetal age and weight in mammals, and we have been assessing both specific foetal growth rates and length of gestation (J. F. D. F. and A. St G. Huggett, unpublished data). It is quite clear that in the higher primates the foetal growth rate is 0.06. Using this and the estimates of foetal sizes at birth in the Huggett/Widdas formula[2] we obtain gestation periods for *A. africanus* of 257 days and *A. robustus* 300 days.

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Measurement of the Diffusion Coefficient in the Concentrated Phases of the Soap-Water System by Nuclear Magnetic Resonance

A MEASUREMENT of the lateral diffusion coefficient of spin labels in lecithin bilayers has been reported by McConnell et al.[1]. This diffusion is found to be rapid, the consequences of which, in terms of the structure of biological membranes, cannot be overlooked. Here we report the result of nuclear magnetic resonance measurements on the diffusion coefficient in the concentrated phases of the potassium laurate–heavy water system. Our results strengthen the theory that diffusion in lipid water systems is rapid, magnetic resonance measurements have the advantage that it is the diffusion of the constituent molecule itself that is being observed and not the diffusion of an added "impurity" as is the case with spin label experiments.

The usual procedure for measuring diffusion by magnetic resonance is to observe the decay of the spin echo in the pulse sequence 90°, τ, 180° as a function of τ, or as a function of the applied magnetic field gradient. This method is valid only for the inequality $12/\gamma^2\ G^2\ D \leqslant T_2^3$ being satisfied where γ is the magneto-gyric ratio of the resonant nuclei, G is the applied magnetic field gradient, D the self diffusion coefficient and T_2 the nuclear transverse relaxation time. This condition is normally satisfied for liquids of low viscosity where the diffusion is fairly rapid and the transverse relaxation time T_2 is of the order of the longitudinal relaxation time T_1. In the concentrated phases of amphiphile–water systems the T_2 is normally too short, owing to dipole–dipole interactions, for a liquid echo, and hence a diffusion coefficient to be obtained by this method. One method of overcoming this difficulty is measurement of the stimulated echo, first described by Hahn[2] and further developed for diffusion measurements by Tanner[3].

To obtain a stimulated echo a sequence of three 90° pulses is required. The echo which occurs an interval after the third r.f. pulse equal to that between the first two pulses is unique in that its relaxation attenuation has a T_1 dependence as a function of the interval between the second and third r.f. pulses. The attenuation of the stimulated echo in this case is given by

$$\ln(M/M_0) = -\frac{(\tau_2 - \tau_1)}{T_1} - 2\frac{\tau_1}{T_2} - \ln 2 - \gamma^2 Dg\tau_1^2\ (\tau_2 - \tau_1/3)$$

where M_0 and M are the nuclear signal initially and at the time of the echo maximum respectively, τ_1 and τ_2 are the time intervals between the first and second, and first and third r.f. pulses. An additional condition discussed by Tanner[3] for optimizing the three 90° pulse sequence for minimum non-diffusional attenuation at fixed diffusional attenuation is that $\tau_2/\tau_1 = T_1/T_2$; also, as the attenuation depends on τ_1^2, this quantity cannot be made too small and in practice must remain a few milliseconds. Thus if the ratio of T_1/T_2 is large, the interval τ_2 must be large and this can cause problems of signal to noise ratio and often, as in our case, demand that signal accumulation and averaging techniques be used.

The results on the potassium laurate–heavy water system prove interesting. In this system, X-ray work[4] has shown the existence of a cubic phase. This phase is unique in that the absorption lines are so narrow that the spectrum can be studied by high resolution n.m.r. The spectrum is in fact very similar to that obtained in the micellar phase. This liquid-like behaviour is due to the complete averaging of the static dipolar interactions. Thus in this phase a liquid echo may be obtained by the sequence 90°, 180° and a diffusion constant measured. This has been

done by Charvolin (J. Charvolin and P. Rigny, to be published) who finds a diffusion coefficient at 80° C of 2×10^{-6} cm² s⁻¹. Charvolin discusses the possibility of fast diffusion in the other concentrated phases. Here we have by means of the stimulated echo technique been able to measure directly the diffusion coefficient in both the hexagonal and the lamellar phases of the potassium laurate system. The results are a self diffusion coefficient of 2.3 $(\pm 0.3) \times 10^{-6}$ cm² s⁻¹ in the hexagonal phase and 2.4 $(\pm 0.35) \times 10^{-6}$ cm² s⁻¹ in the lamellar phase at 80° C. Concentrations were in the hexagonal phase 50% D₂O, and in the lamellar phase 28% D₂O. The temperature of 80° C was chosen because it is above the Krafft point for all phases. On decreasing the soap concentration and passing into the micellar solution, where a liquid echo is observed, the diffusion coefficient rises as a function of decreasing concentration. A factor 3 difference was observed in the diffusion coefficient at 12 g l.⁻¹ and at 120 g l.⁻¹. This is to be expected, for what is now being observed is the diffusion of the micelles themselves becoming more rapid than that of their constituent molecules. A decrease is also observed in the activation energy from 5.7 (± 0.2) kcal mol⁻¹ at 120 g l.⁻¹ to 4.05 (± 0.1) kcal mol⁻¹ at 12 g l.⁻¹. It is interesting to note that the activation energy in the cubic phase is 5.5 (± 0.2) kcal mol⁻¹ (J. C. and P. R., to be published) and in the hexagonal phase is 5.8 (± 0.2) kcal mol⁻¹. This tends to show that whatever macroscopic structure (hexagonal, cubic and so on) the molecular aggregations may take, the motion of the individual molecules remains very similar. We have also examined the diffusion of sodium lauryl sulphate in the hexagonal phase (50% D₂O) and found the extremely rapid diffusion coefficient of 1.6 $(\pm 0.3) \times 10^{-5}$ cm² s⁻¹ at 88° C. An interesting point here which deserves further attention is that in the gel phase of the same concentration (that is at 25° C) the measured diffusion coefficient was 2.5 $(\pm 0.4) \times 10^{-6}$ cm² s⁻¹. This shows a factor 10 difference, and if one assumes a similar activation energy for the process (5 kcal mol⁻¹) then there must be an increase in mobility on passing into the hexagonal phase.

A model which could explain n.m.r. data is that of a molecule whose polar head is constrained to move only in two dimensions, but the terminal methyl group has a completely liquid-like character. Spin-diffusion is not an effective process along the hydrocarbon chain. The T_1 relaxation behaviour is governed primarily by rapid translational diffusion. A certain portion of the chain, however, near the polar head group remains relatively rigid; within this part of the chain, dipolar interactions exist. This gives rise to the T_2 mechanism and also the $T_{1\rho}$.

These results are extremely interesting especially for biological membranes. An ordered system that looks viscous is on the molecular scale behaving almost as a liquid. Examination of diffusion in cell membranes as regards function may throw considerable light on the transport properties.

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BOOK REVIEWS

Unmaking the Mess

The Spoils of Progress: Environmental Pollution in the Soviet Union. By Marshall I. Goldman. Pp. xi+372. (MIT Press: Cambridge, Massachusetts and London, 1972.) £3.60.

The Biology of Pollution. By Kenneth Mellanby. (The Institute of Biology's Study in Biology, No. 38.) Pp. 60. (Edward Arnold: London, November 1972.) £1.50 cloth; 75p paper.

Environment File. Prepared by Michael Hussey for the Technology Foundation Course Team. (The Open University: Bletchley, Bucks, 1972.)

THOSE of us who do not like regimentation often argue that if it were made easier for people to follow their own uncoerced preferences, many of the world's troubles would be ameliorated. It is argued that, if contraception were so perfect and universally accepted that the only babies born were those positively wanted, the population problem would disappear, and that if advertisers stopped foisting new wants on us, we would make much less mess. Goldman does not say anything about population, but he effectively demolishes the illusion that by abolishing advertising we would get rid of pollution. That leaves the abolition as a worthy cause in its own right.

Goldman is connected with the Russian Research Centre of Harvard and shows some sympathy with the initial objectives of the Russian revolution. His book is based on what he saw on many recent visits to the USSR and on intensive study of Russian newspapers and other publications. Although there is little advertising aimed simply at increasing consumption, Goldman makes it abundantly clear that the Russians nearly equal the Americans in their capacity to foul their environment. The main differences he notices are that the atmosphere is less fouled by lead from car exhausts, and there are few abandoned cars and refrigerators. As in other countries, there are laws prohibiting the discharge of noxious effluents, and, as in other countries, they are openly flouted. The Russian "remedy" is to pass a new set

of laws. He notes that Khrushchev introduced more of these laws than Lenin.

In spite of his sympathy with the revolution, Goldman sees ecological disadvantages in the monolithic state. To quote: "Instead of serving as a referee between polluters and conservationists, government officials usually support the polluters. It is necessary to remember that the state is the manufacturer . . .". Sometimes, however, pollution gets so bad that notice has to be taken of it. The result is a fine that can be as small as 5 roubles. To cover any inconvenience that might be caused by a larger fine, factory managers often include a sum to pay the fines in their financial plans at the beginning of the year.

The showpiece in this chamber of horrors is Lake Baikal. Because its water was once pure, a huge mill to produce very high quality paper was built there. It has now so fouled up the water that the site has lost its original merits. Many overlapping commissions were appointed to look into the matter and little attention was paid to their reports. Even the Central Committee of the Communist Party got involved in 1971. It would seem that the USSR has little to learn from Britain about the art of bamboozling the electorate. Russian officials, however, labour under one great disadvantage—the basic documents of their system condemn thoughtless exploitation. Goldman quotes Engels: "Thus at every step we are reminded that we by no means rule over nature like a conqueror . . . our mastery of it consists in the fact that we have the advantage over all other beings of being able to know and correctly apply its laws", and again: "Let us not, however, be very hopeful about our human conquest over nature. For each such victory, nature manages to take her revenge. Each of these victories, it is true, has a first order of consequences which we can anticipate. But in the second and third orders there are quite different, unforeseen effects . . .".

It seems from this book that, in the

USSR, fatheadedness and organizational momentum can do as much environmental damage as cupidity and a wasteful outlook do elsewhere. In Britain, projects such as urban motorways and Concorde get started and then acquire a life of their own that enables them to survive in spite of general disillusionment. According to Goldman, the Russian fetish is damming up rivers ; he quotes the suggestion that the only reason for damming the Ili was that it was the only major river in Central Asia without a dam. Conservationists will join him in lamenting the gradual erosion of Russia's nature reserves. State ownership of land facilitated the establishment of an admirable system. As in other countries reserves have suffered from various forms of industrial encroachment: they have even become private hunting grounds for bureaucrats. But the picture is not unrelievedly black. Municipal central heating is spreading; there is consequently less atmospheric pollution. The area irrigated and fertilized with sewage is being rapidly extended.

The state of the law, and of its enforcement, is part of Mellanby's theme also. He explains that Common Law enables the owner of a stretch of river bank to proceed against anyone fouling his water, and that river authorities could, in theory, clean up the rivers if they moved against the 60 per cent of our urban population that is served by overloaded sewage works. He suggests that this would harm industry and cause unemployment. It is legitimate to wonder whether there would not be compensatory work in bringing the sewage works up to standard and in organizing efficient recycling processes. Mellanby lists some improvements—the Thames is cleaner than it was 20 years ago and smokeless zones make a difference that is obvious to the most casual observer. He deplores both uninformed alarm and uncritical complacency. Thus he urges those who stress only the harm that insecticides can do to consider also the need for them if crops are to be protected and diseases are to be

checked in countries less fortunate than Britain. And he points out that although the amount of lead, derived from doped petrol, absorbed by city-dwellers does not exceed the danger level set by the health authorities, that level may itself be criticizable.

The bundle of eight "exhibits" from the Open University is hard to assess. Some have merely an emotional impact; there is some useful information on the construction and consequences of the Aswan High Dam, and some gloomy forecasts of what will happen if everything goes on happening as it does now. The most valuable "exhibit" is the text of a lecture by Dubos in 1971; he argues that technology should be redirected towards meeting actual human needs, and points out the dangers in oversimplifying both eco-systems and problems.

For as long as an unpleasant state of affairs is regarded as "natural" there is little incentive to do anything about it. With the recognition that it is wholly or in part man-made comes the realization that it could be unmade. We must, therefore, welcome the intensity of discussion on such issues as pollution, ecology and population because, although much nonsense is talked, the fundamental point, that we made the mess and could unmake it, is winning acceptance. The next step, the decision whether the consequences of unmaking are worse than the mess, is more difficult.　　　N. W. PIRIE

Scientific Archaeology

Models in Archaeology. Edited by David L. Clarke. Pp. xxiv+1055. (Methuen: London, November 1972.) £16.

THE editor of this volume, David Clarke, is well known for his book *Analytical Archaeology* (reviewed in *Nature,* **220,** 1357; 1968). This new book consists of twenty-six individual papers especially commissioned by him, each containing in its title the word "model". Together they are claimed to represent "the carefully selected work of progressive archaeologists around the world". The aim of most professional archaeologists today is to set their subject on a broadly scientific as distinct from an entirely subjective basis, and most of the authors in this volume are making a serious attempt to do this.

One possible approach is to tackle archaeological evidence by controlled quantification combined with structure-seeking computer programs. This is a rapidly developing field and relevant papers, for example by G. Cowgill on "Seriation", are serious contributions, although through time lag in publication, not perhaps in touch with the very latest developments. Two attempts to

incorporate such data analytic techniques into specific research projects are rather disappointing through misinterpretations of the published computer output: J. P. White and D. H. Thomas mistake the meaning of two of their three principal components for stone tools, through ignoring the equal importance of negative and positive loadings on such components; L. R. Binford chooses for rotation and interpretation five dimensions of a similar analysis when a simpler solution in two dimensions is indicated. These trivial but rather devastating slips could have been avoided by closer contact with relevant scientific colleagues.

Another related but more ambitious approach to archaeological data is represented by attempts to simulate by computer programming a past human society, so that given data may be replicated by suitable adjustment of the input to the artificial system. So far, no comprehensive results can be reported, but most interesting accounts of work in progress are given by J. E. Doran and D. H. Thomas.

In all of these papers, a "model" may be understood as a mathematical model providing a link between data and interpretation, where the fit of model to data may be specified and assessed. Most other papers interpret "modelling" more liberally. A major preoccupation is seen in locational studies, where geometric patterns are superimposed on known distributions of archaeological sites or features. The need here is to convince the reader that the chosen pattern fits the data better in shape and scale than other obvious patterns that could be tried. When there is no measure of fit, or a realistic null hypothesis (an assumed "random" scatter of points on irregular terrain is hardly a substitute for this), some readers will be less enthusiastic about this approach than others. A similar gap between reality and model is likely to occur when attempts are made to estimate the size of prehistoric populations by calculating quantities of food that could have been produced and consumed. The more cautious locational and demographic studies in the volume, however, are certainly among the most interesting.

Perhaps the least rewarding papers are those that militantly advocate a "new" as against a "traditional" archaeology. This represents a definite school (others have termed it a religion) which claims to have created a new scientific archaeology. Unfortunately, their creed does not depend on the inherent peculiarities and limitations of the relevant data, but on an uncritical allegiance to the tenets of selected philosophers of science. As might be expected, the result is a travesty of both science and archaeology, but it is maintained with

distinct fervour and is given more space and credence than it merits in this volume and elsewhere.

The high point of the volume is undoubtedly E. M. Jope's "Models in Medieval Studies", which demonstrates how many of the more serious techniques hailed currently by prehistorians as "new" have been exploited in a better documented branch of archaeology for decades. Only the jargon was missing. This Jope wittily provides and leaves the reader to ponder whether, after all, the real distinction in archaeology should be drawn not between a traditional and a new approach, but between good and bad scholarship.
　　　　　　　　　　　F. R. HODSON

Nutritional Research

Malnutrition: Its Causation and Control. By John R. K. Robson. In Collaboration with Frances Larkin, Anita M. Sandretto and Bahram Tadayyon. Vol. 1. Pp. x+1–312. Vol. 2. Pp. x+313–613. (Gordon and Breach: London and New York, 1972.) £6.24 for two volumes.

Now that the clouds have lifted from the support of nutritional research, it is time that all the various items of knowledge in this large field were gathered together. This is exactly what these two volumes aim to do; and they succeed. The information is rightly carried into the socio-economic field. Again it is right that the books are dedicated to Professor B. S. Platt. The authors state that they have been "for 18 years engaged in the planning of nutrition programmes at national and local levels and the delivery of nutrition services in the richest and poorest countries of the world". The books cover laboratory as well as field research and teaching. It is accurate for the authors to describe nutrition as based upon "pure, applied and social sciences, including chemistry, biology, physiology, medicine, agriculture, education, sociology, economics, anthropology and politics". So often this is not realized.

In volume 1, the first long chapter deals with global nutrition, the effects of various deficiencies, including trace elements and protein–calorie deficiency, as well as overnutrition. This is followed by a more detailed chapter on the ecology and aetiology of malnutrition, dealing, among other things, with flour, rice, maize, the Irish potato problem and the size of families and weaning. The rest of volume 1 includes a chapter on normal nutrition giving the reader a condensed, but adequate, account of the physiology of the gastrointestinal tract and up to date knowledge of the biochemistry of the cell. In this, attention is given to transport systems, ATP, carbohydrates, fats, pro-

teins and their balance, nitrogen and energy balance, inherited disease, respiratory quotients, calorimetry and the action of vitamins. Useful summary diagrams are included. A valuable feature of both books is the set of references at the end of each chapter.

The second volume starts with a summary chapter on nutrient requirements; pains are taken to explain the different possible meanings of this, and the differences between the minimum and optimum requirements. Attention is given to recommendations of different bodies such as WHO and national schedules. A table gives recommended daily intake of vitamins, iron and protein at different ages. There is valuable critical discussion of tissue depletion, vitamin C and the increased need by elderly folk for thiamin, and the interaction of fats in the absorption of vitamin A.

Chapter 5, running to 108 pages, is occupied with the problem of the assessment of nutritional status, and is in some ways the most important, for the reason that a description is given in critical detail of the various possible approaches and the difficulties under field conditions of arriving at a true assessment. Its wisdom is clearly based upon much practical experience and should be read by anyone who thinks of starting such work. Part 2 concludes with a description of nutrition programmes and service, including problems of education. There is also a fascinating account of food habits, from which most would learn something which they do not know. I noticed with interest that there is no explanation of the replacement of calories by joules; surely it is better not to worry the reader with this new term in place of the universally accepted "calorie".   RUDOLPH PETERS

Mathematical Men

Men and Discoveries in Mathematics. By Bryan Morgan. Pp. xii+235+9 photographs. (John Murray: London, October 1972.) £2.

MORGAN surveys the development of mathematics from antiquity to our times in a style suitable for the layman. Many such books are available now, and they should give this one a rough time, for they normally recount the same material with greater command and accuracy. For example, consider chapters 6 ("The Great All Rounder", referring to Gauss—although the last third deals with other mathematicians) and 7 ("Yesterday and Today"). Among the anachronisms, Gauss's contemporary Babbage is in chapter 7, and is falsely said to be "fifteen years later" than de Morgan; Weierstrass is in chapter 6, before Abel and Galois; and Fourier is a chapter early, in chapter 5.

There are also frequent errors of fact or questionable interpretation. In particular, in one section Morgan misrepresents Cantor's continuum hypothesis and claims that Cantor proved it, asserts that Kronecker's criticisms drove Cantor into a mental hospital, confuses Russell's *The Principles of Mathematics* with *Principia Mathematica*, describes Frege's *Die Grundgesetze der Arithmetik* as dealing with "the logic of classes", asserts that Russell tried to prove consistency, and identifies Gödel only as "an Austrian logician".

It is not worth going on; better to pick up the danger signals at the beginning. For anyone who thinks that M. Cantor's *Geschichte der Mathematik* is "definitive" and E. T. Bell's *Men of Mathematics* is "scholarly" must have a measure of historical command which is "there but not there", to use Morgan's misrepresentation elsewhere of Leibniz's infinitesimals.

I. GRATTAN-GUINNESS

Uses of Groups

The Fascination of Groups. By F. J. Budden. Pp. xviii+596. (Cambridge University: London, August 1972.) £6; $18.50.

THE basic reason for teaching any branch of mathematics to non-specialists is that it provides an appropriate language in which to talk about some interesting and frequently occurring class of phenomena. What that class is, in the case of well established branches, is something that we learn so early that we hardly think about it at all. Even the least numerate person knows that numbers are there for counting and measuring, and has some idea of the situations in which counting and measuring are useful. But with a less traditional subject, such as group theory, the kinds of situation in which the language applies, as well as the truths that can be expressed in it, have to be taught consciously. This is what is meant, in this context, by that rather misleading word motivation. The great merit of this book is that it makes a serious attempt to provide motivation in this sense; no one will learn much group theory from it, but anyone who reads it carefully will end up with some idea of what group theory is about. I doubt Mr Budden's claim that his book will be of use to university students, but I would expect it to be indispensable to teachers of mathematics in schools, and of immense value in school libraries.

What the book does first is to take the two ingredients of a group, a set and a binary operation on it, and the four conditions imposed on them, the closure and associativity of the operation, and the existence of a neutral element and of inverses, and to examine them in turn, with a wealth of examples, chosen to show what the definitions exclude as well as what they include. The same detailed treatment is then given to such basic concepts as the order of an element, isomorphism, subgroups, direct products, and homomorphisms, and to the simplest classes of groups, cyclic groups and dihedral groups. Finally, there are four chapters on applications, to music, to bellringing, in geometry, and to plane symmetries. The chapter on applications to music includes an interesting example of motivation; namely, the relation between equally tempered and natural scales. One can think of the natural scales as reality: equal temperament is a mathematical construct, which simplifies reality at the cost of some distortion, and the simplification consists in this, that the set of intervals is now closed under the appropriate composition, and so forms a group.

I found the book irritating in places. Why, for example, should two successive chapters be labelled "Cyclic Groups" and "The Dihedral Group" when it is clear that on any interpretation there are just as many dihedral groups as cyclic ones? More seriously, it is a pity to state on page 410 that Galois proved that the alternating group A_n is simple for $n \geqslant 5$, and to suggest on page 411 that we do not know whether there is an infinity of finite simple groups. Again, it is perfectly reasonable to ask the reader to show that the relation $r^4=1$ is a consequence of the relations $ar=r^3a$ and $a^2=r^2$, but, for the sort of reader at which it is aimed, it seems too hard to be asked to prove that $r^4=1$ and $ar=r^3a$ do not imply $a^2=r^2$. At the very least, he should be asked first to consider carefully what sort of argument could possibly prove such a non-implication.

But these are minor blemishes. The book's only major blemish is its price.

GRAHAM HIGMAN

Echinoderms

Physiology of Echinoderms. By John Binyon. Pp. x+264. (Pergamon: Oxford and New York, October 1972.) £4.80.

THE current spreading of interest in echinoderms, together with the physiological emphasis of many undergraduate courses in zoology, has created a need for an up-to-date review of the subject. The various chapters cover most aspects of echinoderm physiology, and Dr Binyon has used his knowledge and experience to provide a direct account of the topic.

The chapters on excretion, osmo-regulation, biochemical affinities and respiratory physiology give useful surveys, but others are not so up to date. Important work has been carried out on feeding, digestion, chemical composition, toxins, sensory physiology, the excitable tissues, the water-vascular system and on spawning and neurosecretion which is not treated by the text. Of the references cited there, less than 5 per cent concern papers published after 1966, the date of the previous review of the subject. The author has provided an addendum of about 250 references, mostly to work carried out between 1966 and 1970, but these are not dealt with by the text so they merely direct the reader to possible sources of information.

Echinoderms constitute a singular group of animals, and many aspects of their biology are unique. Consequently the book would have been improved by the inclusion of an adequate introductory chapter. Readers not familiar with the phylum may have some difficulty with unexplained terminology, and little guidance is given on the organization and classification of the group. Although the author stresses that the unusual symmetry and the absence of a head have influenced the development of certain physiological systems, he might have emphasized other significant features that echinoderms display. These include the exclusively marine habit, the large coelom and the unique skeleton.

The usefulness of the book could have been increased if it had been planned differently. As it is, some information that would be of use earlier in the text is withheld until later and the headings and cross references do not always lead one to the expected information.

While this book will be valuable for some aspects of undergraduate work, it will be of limited assistance to the researcher because it is out of date in several respects.

ANDREW C. CAMPBELL

Viruses of Man

Strains of Human Viruses. Edited by M. Majer and S. A. Plotkin. Pp. x+271. (S. Karger: Basel and London, 1972.)

THIS book fulfils a long standing need in virology. Edited by M. Majer and S. A. Plotkin, with individual chapters contributed by different workers, it is a catalogue of the strains of human viruses which are either official prototype strains or which have been widely used by workers in the fields involved. Strains used for vaccines and those with genetic markers are also listed. In each

case, the source of the original isolate and the laboratory where the first isolation was made are given together with the passage history and a summary of the characteristic features of the strain. No book, of course, is perfect, and it is a real pity that in most instances there is no mention of the laboratories from which the viruses may be obtained. References to the literature on each strain are given which the editors suggest should be consulted for this information, but this is much less useful than a list of laboratories which stock the strain concerned. The editors also make apologies to "the scientist whose pet strain has been omitted" and there are certainly a few surprising omissions some of which will no doubt be corrected in a second edition. A more serious criticism is that in the chapter on herpes simplex virus it is not always stated if the strain is type 1 or type 2. In cases in which serological typing has not been done this should have been stated—although it is doubtful if such a strain merits inclusion at all. These criticisms, however, are minor and do not seriously detract from an exceptionally useful book. It will undoubtedly become an indispensable reference book in all virus laboratories.

MORAG C. TIMBURY

Plant Hormones

Plant Hormone Research in India. By S. M. Sircar. Pp. vi+264. (Indian Council of Agricultural Research: India, New Delhi, 1972.) Rs. 12.50.

THIS is a comprehensive volume, divided into three parts. The first provides a general account of plant hormones including historical aspects, terminology, chemistry, methods of application and mode of action. The second part is concerned mainly with the practical uses of hormones and, in addition to well known applications such as rooting, fruit setting and weed control, the effects of hormones on plant metabolism and their role in promoting growth of plant tissues and organs in sterile culture media are discussed. An account is also given of hormone inhibitors and growth retardants. In the third part of the book the author considers the potentials of growth hormone research. There is a chapter dealing with hormones in tropical plants in which particular attention is given to the results of Indian workers. The final chapter considers the importance of hormones in bud, stem, and fruit growth, abscission of leaves and fruit, and senescence.

Apart from the special attention given to Indian plants there is nothing very novel about this book. However, it is

quite well produced, with useful photographs, diagrams and an extensive bibliography and it has brought together most of the important findings of hormone research. Because of its special emphasis on local plants and crops it will be especially useful to botanical and agricultural students in India.   R. L. WAIN

Pictures of Rocks

The Minor Structures of Deformed Rocks: a Photographic Atlas. By L. E. Weiss. Pp. vii+431. (203 plates.) (Springer: Berlin and New York, 1972.) 94 DM; $29.80.

THIS unusual book, which has been described as an atlas, contains more than 200 full or half-page plates with brief paragraphs, stating the types of structures, rocks and localities illustrated; a brief six-page introduction is followed by a further twelve pages, entitled "Introduction to Plates", two pages of references and a short subject index completes the text.

The author states that the main aim of the book is merely to illustrate the common minor structures resulting from rock deformation. The interpretation of such structures is left to other texts. For my part, I cannot agree with the author when he asserts that most field geologists are not and should not be concerned with the mechanical problems of rock flow. I believe that most people only "see" those things they understand, or think they understand. To this end I would have liked to see more interpretation in this book.

This apart, the book stands or falls on the coverage of material and the standard of photographic reproduction. The work contains about fifty plates illustrating planar features, more than seventy on folds and almost eighty further plates dealing with lineations, boudinage, veins and "complex" structures. The author freely admits that these structures represent his main interests and he has made no effort to include coverage of faults and joints, an omission which I find regrettable. The quality of the photographic content, which is due wholly to the author, and of the reproduction, ranges from acceptable to excellent, with a preponderance of the latter.

This work will doubtless be used by students as a "photographic" dictionary —a form of Duden—and, in addition, I am sure that teachers of structural geology around the world will contravene the laws of copyright and reproduce many of the plates presented, to augment their own teaching material.

NEVILLE J. PRICE

Primate Atlas

Taxonomic Atlas of Living Primates.
By A. B. Chiarelli. Pp. vii+363.
(Academic: New York and London,
August 1972.) £6; $18.50.

THE principal features of this atlas are
an identification key and a series of
species profiles providing information
on distribution, body weight and size,
coat coloration, synonyms and verna-
cular names. Most profiles have
accompanying photographs and com-
bined distribution maps are included.
Attractive though this schema might
appear to be, its realization sadly leaves
much to be desired.

The basic classification itself would
find few adherents today. Recognizing
only suborders, families, genera and
species, the author has his first suborder
Prosimii embrace Tupaiidae and
Tarsiidae as families of equal rank to
five lorisiform and lemuriform families.
At lower levels the general absence of
subgenera and species groups, combined
with some tendency to "lump", has
meant the virtual disappearance of cer-
tain significant distinctions (for example,
Miopithecus) and indications of special
affinity (for example, among *Presbytis*
species).

The identification key, while useful,
is not without errors and its effective-
ness is curtailed where, in spite of the
claim to be based upon readily recog-
nizable external features only, it relies
on a knowledge of dental characteristics,
the pelage colour of the neonate or the
animal's provenance.

In the profiles of the individual
species carelessness is everywhere
apparent: mistakes and inconsistencies
abound, and the brevity of treatment is
such as to make many statements posi-
tively misleading. Weights and linear
measurements are given without refer-
ence to sample size so that a range may
in fact derive from only two animals,
and a single figure may be either an
average or a measurement from a single
individual. Neither here nor elsewhere
is there any indication of the extent to
which subspecific variation occurs and
affects the issue.

The descriptions of coat colour
repeatedly fail to characterize ade-
quately the species and the sections
dealing with geographical distribution
are no more satisfactory. Why are
some ranges specified precisely but
others given only in general terms?
More disturbing is the frequency of
errors in distribution data in both text
and maps; examples are species of the
genera *Tupaia, Papio, Presbytis,
Colobus* and *Hylobates,* but many more
could be cited.

Finally, too many photographs are
of unnecessarily poor quality and line
drawings have been used in some in-
stances when very good photographs

exist. And the last thing one expects
in a taxonomic atlas is the incorrect
identification of photographs, yet this
fault appears at least twice: the picture
presented as *Tupaia ellioti* is not of that
form (*Anathana*) but probably shows a
southern *T. glis*; the so-called
Microcebus murinus is really an infant
Galago senegalensis.

One must conclude that although this
work does serve a useful function even
as it stands, it would have been so much
better had more care been taken in its
compilation. G. H. MANLEY

Reproduction

Reproductive Patterns. Edited by C. R.
Austin and R. V. Short. (*Reproduction
in Mammals, Book 4.*) Pp. vii+156.
(Cambridge University Press: London,
1972.) £3.40; $11.95.

Artificial Control of Reproduction.
Edited by C. R. Austin and R. V. Short.
(*Reproduction in Mammals, Book 5.*)
Pp. 152. (Cambridge University Press:
London, 1972.) £3.40; $11.95.

SCIENCE is usually written about either
in a formal style by academics or in a
more racy and provocative style by
journalists. These two volumes, con-
cluding the series *Reproduction in
Mammals,* follow their predecessors in
combining many of the attributes of
both. Written by acknowledged experts
in a lively and immensely readable
fashion they cannot possibly fail to
fan the interest of anyone with the
least spark of curiosity about repro-
ductive biology. The various authors
have extracted their information from
reliable and comprehensive sources,
including their own contributions, and
presented it in an uncluttered form
with clarity and coherence. The
numerous tables, graphs and line
drawings have generally been used to
good effect. In the many instances
where different topics overlap there is
a reference to other chapters in the
series, and a sensible short reading list
is given at the end of each chapter.
The editors' brief was clearly to con-
sider the human angle wherever pos-
sible, and this has been done by refer-
ence to known facts, and also by extra-
polation and prognostication.

The authors have stood back from
the trees and shown us what the wood
really looks like. This is an ideal
approach for newcomers to the subject,
as well as for their teachers, and also
serves as a useful compass for those
who may have got lost in the depths.
In the absence of any serious competi-
tion at this level of analysis these
volumes are to be welcomed as a valu-
able addition to the teaching texts. And
even student grants would run to the
paperback issues. In some ways the

whole series might have been better
published as a single volume, but this
is a purely personal view.

The volume on reproductive patterns
is not so restricted as the title might
suggest, and as well as articles on species
variation, environmental control and
behaviour, there is consideration of
immunological factors and of ageing.
The whole is illustrative of the diversity
of control processes in reproduction
both within the individual and the
society.

In the final volume stress is laid upon
the pressing dual requirements for in-
creasing farm animal production whilst
severely limiting human reproductive
potential. Hopes for the former are
high, but there appears to be much less
optimism for a significant assault on
the latter. In all likelihood we shall
have to rely on the perfection and appli-
cation of presently available methods
of contraception rather than hope for
the development of any totally new
ones, at least for a solution to the prob-
lem in the foreseeable future. The fe-
male of our species will be particularly
dismayed to learn that there is no imme-
diate prospect for a chemical method
of male contraception.

It is often forgotten that for the in-
dividual problems of infertility and
developmental abnormality are con-
sidered more urgent and distressing. The
achievements and aspirations in these
areas are also dealt with in this volume.

The series editors themselves con-
clude with frank discussions of the
social, ethical and legal implications of
manipulating human reproduction.
Their stand is uncompromising. The
present situation demands that we alter
those attitudes that have been forged
by cultural and religious dogma and
assume full responsibility for the ex-
ploitation of new scientific techniques.
 W. D. BILLINGTON

Finches of Europe

Finches. By I. Newton. Pp. 288+28
plates. (William Collins: London,
February 1973.) £3.

THIS is an excellent account of the
European representatives of an interest-
ing group of small, stout-billed, seed-
eating and often brightly coloured birds
—the true finches (Fringillidae). There
are two subfamilies, one comprising
only the chaffinch, the brambling and
a single extralimital form; the other,
the cardueline finches, has well over a
hundred species, of which sixteen are
European. Much of the book is based
on Dr Newton's own researches, but he
has also made full use of the extensive
literature.

Three chapters are devoted to a sum-
mary review of the eighteen species.
Most of the others deal more generally

with different aspects of finch biology, taking examples from here and there and comparing one species with another. This is a valuable presentation, much that is said having a wider application than merely to the particular group. Geographical distribution and habitat preferences provide one aspect, and it is interesting to note the changes that have taken place in recent years in adaptation to the effects of human activities on the environment.

Feeding ecology is rightly given a prominent place. No two species of European finch have identical feeding habits; they differ in the sizes of seeds that they prefer and in the types of seed-head that they can best exploit, and these are related to the precise structure of the bill and to the particular method of using it. Nevertheless, new feeding habits can arise and spread through the population. The special feeding habits of the bullfinch have made it a major pest in orchard areas.

Further chapters deal with social behaviour, breeding, moult, migration and irruptions, and body weight. We are given an able statement of modern views on migration, applicable not only to these birds but largely to "hardy" migrants in general. Those finches that depend on the seeds of a few tree species, as contrasted with those dependent on herbaceous plants, show great differences in their movements from year to year in relation to a sporadic food-supply. The crossbills are a special case, moving only once a year and taking up new breeding areas.

The book is well illustrated with colour plates, photographs, drawings and clear maps and diagrams.

A. LANDSBOROUGH THOMSON

Heathland Microcosm

Ecology of Heathlands. By C. H. Gimingham. Pp. xv+266. (Chapman and Hall: London, October 1972.) £4.75.

As Professor Gimingham explains in his introduction, he has concentrated on certain aspects of the heathland ecosystem, in particular the vegetational components, but the lack of a detailed zoological treatment should not deter any ecologist interested in this subject. He has presented heathland as a microcosm. This feature alone makes his book different from the many ecological texts which rely on disparate examples: he is able to illustrate the whole range of plant ecology by reference to this particular vegetation type.

The characteristics of the plant, in particular its mode of growth, are shown to determine the nature of heathland and are related to such features as the current pattern in the vegetation, both short-term and longer-term history,

management practices, as well as the responses of the larger animals and even the physiological behaviour of the heather plant.

This dynamic interrelationship is a refreshing change. Recently the sledge-hammer of numerical techniques has flattened the descriptive part of ecology; Professor Gimingham shows us what has been lost. In particular the chapters on growth form in relation to community structure, cyclical processes, management by fire and for grazing, nutrient cycling and conservation, make fascinating reading and exemplify this dynamic approach to the system.

I have only a few minor criticisms of this book. There is the usual crop of misprints, particularly in tables, and an unfortunate transposition of lines on the inside flap of the dustjacket—the part that most people will read first. In the chapter dealing with the phytosociology of heathlands, the reader might be forgiven for gaining the impression that, except for communities dominated by tree heaths, the southern limit of heathland is France. Many of the heath types (for example, *Calluna-Ulex* heaths, *Erica vagans* heath, humid heath with *Erica ciliaris*) all extend into the north and west of the Iberian peninsula; in fact, some of these have their phytogeographical centres in northern Spain. I should also have liked to see an expansion of the chapter on physiological ecology, perhaps particularly with regard to recent work on the photosynthetic behaviour of heather, although I must admit that this probably reflects only my personal bias.

In conclusion, I warmly recommend this book, not only to students of heathland, but also to anyone interested in ecology. It is a masterly analysis and exposition of ecology as the science of interactions. P. BANNISTER

Has Man a Future?

Conservation for Survival: An Ecological Strategy. By Kai Curry-Lindahl. Pp. xiv+335. (Victor Gollancz: London, October 1972.) £3.25.

THE author of this book is a well-known Swedish zoologist who has taken an active part in international conservation activities, particularly in Europe and Africa. He has now taken a very broad and penetrating look at the world's problems and finds few crumbs of comfort in a long catalogue of man's folly. The first chapter is a global sketch of man's place in the world and his impact on the environment; chapters 2-8 consider the "Air", "Sea", "Fresh Water", "Soil", "Vegetation", "Animals", and "Man", while the last four discuss "Is Conservation a Losing Battle?", "Continental Problems of Today", "The Future" and "An Ecological

Strategy". Dr Curry-Lindahl's treatment of these subjects is probably more comprehensive than previous books of this type and the layman, for whom it was written, might find that there is too much for his mental digestion while any particular section which interests him is likely to be too brief. There are, for instance, 126 separate headings in 312 pages allowing 2.4 pages per subject. The simplification of ecological phenomena, which is perhaps inevitable in a popular book, leads to over-optimism in some cases (the value of biological control and the use of natural herbivores in Africa in preference to domestic stock, as a source of protein) while, elsewhere, the accusation might be over-pessimism, for example the alleged inability of food supplies to increase as rapidly as the predicted population expansion. Nevertheless it would be wrong to dismiss this book as just another of the many which have appeared in recent years on the evils of overpopulation and consequent environmental degradation. The reader feels entirely sympathetic to the feeling and understanding displayed by the author as he presents his case and the constructive points which are made in the final chapters.

There would be much agreement, for instance, for the view that too many of the politicians, planners and economists, who make decisions affecting us all, behave as if the size of the GNP is the only thing which determines the quality of life and that the standard of living can only be measured in economic terms because "progress" is equated with technological advance which is motivated by profit. The author asks for the formulation by the UN of "a world policy of management and utilization of renewable natural resources". This, he says, should be drawn up by a council which would be the highest international scientific authority on the conservation of nature and environmental problems. These are brave words but the history of action by the UN in other matters makes the mind boggle at the scale and extent of world catastrophes which would be needed to overcome the natural inertia of this organization. It seems that men of power find the needs of tomorrow too difficult to solve and so fall back to the events of today because it is the only ground they have to stand on and yet are unaware that it is slipping away from under their feet.

The book is provided with a glossary and "select bibliography" which includes the major books consulted and a selection of publications which appeared after the completion of the text. The references to original papers consulted were deleted by the author from the bibliography, at the publisher's request, but no one seems to have noticed that they still remain in the text.

ERIC DUFFEY

CORRESPONDENCE

Extraterrestrial Intelligence

SIR,—Nobody, it is to be hoped, now believes that the question, how many angels could stand on the head of a pin, used to be a standard topic of debate among the Schoolmen. Tenth-rate philosophers, then as now, may, of course, have debated many senseless things; but to suppose that men of the calibre of Albertus Magnus or St Thomas Aquinas would have wasted their time on such nonsense is absurd.

Yet the Schoolmen at least had this much on which to go, if they ever did consider such a question: they knew that the angels existed—or, at least, they thought that they knew it. But what is to be made of it when, in these enlightened times, men discuss things in the existence of which they have no real reason to believe? I am thinking of discussions about civilizations, or intelligent beings, outside the Earth, as for example in Walker's recent article (*Nature*, **241**, 379; 1973).

There is not, I suggest, a single bit of evidence to show that there is any likelihood that such things exist. What do we know about the matter? In the Solar System, every piece of new evidence makes it seem less and less likely that there are living beings of any kind, let alone intelligent ones, outside the Earth. As for hypothetical systems associated with other stars, we know—nothing. That there are binary stars, the members not necessarily of equal brightness or temperature, we know. It is quite possible that, in some cases, one of the pair might be relatively cool and small; and there may be some observations to support such a notion. But observations from a distance on our own Sun, if precise enough, would show that Jupiter is here. From what we see of Jupiter and the other giant planets, it would seem that, if there are planets around other stars, the more likely they are to be detected the less likely they are to be suitable homes for living beings. And even if matters of size and temperature could be resolved, we are, needless to say, far from finding out anything about the chemical composition of such hypothetical planets. But the composition is crucial to their suitability as homes for living beings.

Besides, the supposition that there are such intelligent beings in such situations depends on the supposition that intelligence will, somehow, arise of its own accord. But in any such view there are extremely grave philosophical difficulties, as even Darwin admitted.

So why do we not, for the time being, put a little more imagination into our discussions of extraterrestrial civilizations—we have nothing else to put into them anyway—and call them science fiction? If, then, the day should come when we have some sober facts on which to go, we could begin to call the result sober science.

Yours faithfully,
H. L. ARMSTRONG

Department of Physics,
Queens University, Kingston, Ontario

Neolithic Garden of Eden

SIR,—Mr Macy asks why, if one assumes the concept of a creator, should one then accept the idea of "fixed laws", such as gravity (*Nature*, **242**, 73; 1973). In answer, I suggest that he reads what Whitehead, Collingwood, Butterfield and Hookyaas have to say about the influence of religion on the rise of modern science. They conclude that belief in the Christian doctrine of the creation of an orderly universe by a rational God helped provide a philosophical climate in which science could flourish. It gave Kepler, Newton and so on a basis for belief in the existence of "natural laws" for which they could therefore confidently search.

If I understand him correctly, Mr Macy then says that religious and scientific models of the universe are "contradictory". Surely the word he should have used is "complementary"? The aim of religion is to understand the meaning and purpose of the universe. The aim of science is to understand its mechanism. This is why those who try to build a world view on a purely scientific basis often conclude, as they logically must, that there is no meaning or purpose to the universe. This does not prove that there is no purpose to it, only that the concept of purpose is excluded from science by its terms of reference. The complementary, and compatible, nature of Christianity and science is shown by the fact that modern science rests on a philosophical basis borrowed from Christian theology. As Collingwood has said "The presuppositions that go to make up this Catholic Faith . . . have as a matter of historical fact been the main or fundamental presuppositions of natural science ever since"[1]. The major points of conflict between Christian theology and science have been at points where the former had, unfortunately, been adulterated by Aristotelianism.

When Mr Macy says that the book of Genesis must be taken as poetical, I presume that he is referring only to the creation story. From chapter 12 onwards the archaeologist Albright can say "But as a whole the picture in Genesis is historical"[2]. Even if the creation story is poetry, that does not exclude it from having a factual basis. What impresses me about it is how well it agrees with the available evidence. This is even more remarkable when one compares it with the fantastic nature of the other extant creation stories from the Near East. The order of creation given in Genesis is in general accord with the fossil evidence. Pearce[3] has pointed out that chapters 2–4 agree well with what we know about the rise of neolithic culture in the Near East. Thus Adam and his immediate descendants are presented as stone age people (the first use of bronze is noted some generations later, in chapter 4, verse 22) who were agriculturalists living in settled communities. The origin of this culture is given as the Garden of Eden. The geographical position given for the Garden puts it in the area from which neolithic culture spread into the Middle East and Europe. It seems to me that far from being something to be sneered at or ignored the early chapters of Genesis form a very remarkable document, both from a historical and religious point of view, and they deserve to be taken seriously.

Yours faithfully,
E. C. LUCAS

The Dyson Perrins Laboratory,
South Parks Road, Oxford OX1 3QY

¹ Collingwood, R. G., *Essays in Metaphysics*, 227 (Oxford University Press, Oxford, 1966).
² Albright, F. W., *The Biblical Period from Abraham to Ezra*, 5 (Harper and Row, New York, 1963).
³ Pearce, E. K. V., *Who Was Adam?* (Paternoster Press, Exeter, 1969).

Square Cylinder

SIR,—A "cylinder" of square cross section. So the Cambridge applied mathematicians and/or theoretical physicists[1] have squared the circle or have they cibed the cylinder?

This is a protest against the misuse of universally accepted terms. A cylinder is essentially circular and cannot have a square cross section in the sense used. The body was apparently a right prism of square cross section or in common terms a square bar.

Yours faithfully,
P. B. N. NUTTALL-SMITH

21 Hall Lane, Yateley,
Camberley, Surrey

¹ Mulhearn, P. J., *Nature Physical Science*, **241**, 165 (1973).

HeLa

SIR,—I was pleased to read J. Douglas's question, "Who was HeLa?" (*Nature*, **242**, 144 ; 1973).

I came across a poem by Nancy L. Caroline called "To Helen Larson" (*Perspectives in Biology and Medicine*, **15**, 1971). It ends : —

Then Helen Larson wed. Her groom
Was cancer. Soon she felt
Death stirring deep within her womb.
She never tried to be immortal. She
    died
Respectably but in her dying
Quite untied the knot of sex and death
Her breath ceased
In the tomb
Unmindful that her womb persisted
    separately.
To multiply is to divide
Spawning immortality.

Yours faithfully,
                              P. P. GIORGI

Medical Research Council
Demyelinating Diseases Unit,
Newcastle General Hospital,
Westgate Road,
Newcastle upon Tyne NE4 6BE

Sense on Pollution

SIR,—Bearing in mind your obviously very deeply felt and persistent opposition to all things environmental, I suppose one must excuse the inaccuracy of the underestimate of current public concern about the environment implicit in your editorial "Measured Sense on Pollution" (*Nature*, **241**, 489 ; 1973). What is much less excusable, however, is your assertion that "it has long since become apparent that British government depart-

ments are well equipped to take environmental problems in their stride". Since I find it impossible to believe that you could be so naive as seriously to consider that the British government and its civil servants, highly competent and widely experienced though they indubitably are, are presently equipped to cope with the manifold current and future environmental problems associated with population growth, increasing usage of dwindling natural resources, pollution and the need for adequate food production, I am bound to deplore the cynicism of your statement.

I am inclined to suspect that your ostensible claim that the bureaucrats will see us through, come hell or high (dirty) water, is in reality a restatement of the irresponsible and untenable view that, no matter what problems science and technology confront us with, technology and science will come up with a solution, the problematical side-effects of which will be solved by science and technology . . .

Yours faithfully,
                          PETER FERDINANDO

202 Carlton Road,
Gidea Park,
Romford,
Essex

Announcements

International Meetings

April 4, **Third Weizmann Institute Lecture on "Membranes, Natural and Manmade"** (Weizmann Institute Foundation, Rex House, 4/12 Regent Street, London SW1).

April 15–19, **Third Conference on Recent Advances in Bio-Medical Engineering** (John D. Gasking, Dept of Pharmacology, The Medical College, St Bartholomew's Hospital, Charterhouse Square, London EC1).

Erratum

IN the News and Views article "Infection in Pregnancy and Foetal Growth" (*Nature*, **241**, 425; 1973) our correspondent regrets that the work of Coid and Ramsden (on page 460 of that issue) was incorrectly quoted. The last sentence in the first column should read "The ratio of serum albumin to $\alpha 1$ foetoprotein was lower in the newborn mice which were growth retarded . . .".

Reports and Publications

not included in the Monthly Books Supplement

Great Britain and Ireland

Scientific Proceedings of the Royal Dublin Society. Series A. Vol. 4, No. 22: An Altitudinal Sequence of Soils in the Sutton-Howth Area of Co. Dublin. By B. O'Flynn and J. F. Collins. Pp. 315–330. 50p. Vol. 4, No. 23: The Life Cycles of Some Invertebrates in an Isothermic Stream in Western Ireland. By Edward Fahy. Pp. 331–342+plate 14. 50p. Vol. 4, No. 24: Palaeomagnetic Results from Irish Carboniferous and Triassic Rocks. By F. G. Mulder. Pp. 343–350. 50p. Vol. 4, No. 25: Growth Trends of Zircons from the Northern Part of the Leinster Granits. By L. N. Gupta. Pp. 351–370. 50p. Series B. Vol. 3, No. 10: Observations of Some Fusarium Populations in Co. Donegal Oat Soils. By M. J. Downes. Pp. 127–136. 30p. Vol. 3, No. 11: The Reclamation of Mountain Soils and Attendant Profile and Land-Use Changes. By Michael J. Conry. Pp. 137–158+plate 2. 75p. (Dublin: Royal Dublin Society, 1972.)   [241
University of Oxford. Schedules of Lectures Authorized by Boards of Faculties, Hilary Term 1973. (Lecture Lists Supplement (2) to *Oxford University Gazette*, Volume CIII.) (Oxford: The University, 1973.) 20p.   [241
Radiopharmaceuticals and Clinical Radiation Sources, 1973/4. Pp. 91. (Amersham: The Radiochemical Centre, 1973.)   [261
National Survey of Air Pollution, 1961–71. Vol. 2: South West Region ; Wales Region ; North West Region. (Warren Spring Laboratory, Department of Trade and Industry.) Pp. viii+198. (London: HMSO, 1972.) £3.50 net.   [261

What Future for Energy ?

IT is no accident that the United States has slipped from preoccupation with what used to be called an environmental crisis to preoccupation with the now more topical energy crisis. In many significant ways, the restrictions on development which have been adopted in the past few years, on the deployment of nuclear power stations and the exploitation of off-shore petroleum reserves, not to mention the restrictions coming into force on the design of automobile engines, have helped to diminish the supplies of several fuels. In several states, for example, there is already talk of gasoline rationing during the coming year--the oil companies are telling distributors that they will have to be satisfied with as much gasoline as they were able to sell last year. The reasons appear to be more a consequence of a shortage of refining capacity and distribution facilities than of a physical shortage of crude petroleum. The coming year is also likely to see further restrictions in the United States on the use of natural gas, if only because the plan to import this material in liquid form from North Africa—the formal agreement was signed only last week between a consortium of American utility companies and the Algerian Government—will not begin to yield deliveries of natural gas until 1975. Then the shortage of electricity—and the prospect of load-shedding in the summer—is likely to continue at least until the electricity utilities can recover the ground lost in the past few years by the difficulty of finding sites for generating stations, conventional and nuclear. In all the circumstances, it is high time that the United States took a firmer grip on these problems and, in particular, that it should distinguish more clearly between the present "crisis" and the more distant problem of how to keep itself adequately supplied with energy.

The starting point for these discussions is, or should be, clear recognition that it is not possible to transform the character of an industrial economy overnight, by the enactment of legislation. The consumption of energy in the United States is much greater than in other countries, and has for the past few years been increasing as quickly as in any closely comparable economy. Between 1971 and 1972, the total consumption of energy in the United States increased by 4.9 per cent and, because of the inevitable limitation of domestic supplies of hydrocarbon fuels, imports of all kinds of fossil fuels increased by 24.5 per cent in the same period, with the result that imported fossil fuels now account for more than 12 per cent of all the energy consumed in the United States. There is no great surprise in these figures. Indeed, what is happening now in the United States is very similar to what happened in Britain and other European countries in the mid-1950s. Supplying a rapidly growing economy from exclusively domestic fuels is bound to be difficult, not merely because of the problems of maintaining capital investment in fuel extraction processes at a sufficiently high level but also because there are positive advantages in the kind of flexibility which a substantial import programme provides. And the truth is that for the time being, there can be no

marked change in the pace of growth of the demand for energy without a radical and often painful change in the pattern of energy consumption.

How is this to be done? In spite of all the breast-beating about the energy crisis now in vogue, the mechanisms for regulating demand remain much as they were when Adam Smith first outlined the operation of the laws of supply and demand more than a century ago. Energy remains an exceedingly cheap commodity in the United States. The retail price of petrol in Europe is 2.5 times the retail price of gasoline in the United States, even after the recent bout of price increases. Is it unreasonable that there should now be a steady increase of price? Such a development is, for one thing, inevitable as the proportion of imported petroleum increases. Its immediate consequence could be a beneficial economy in the use of gasoline, and there is even a possibility that some of the freight now transported across the United States by road would find its way back to the railways, which are even more acutely in need of the business than they have ever been. The price mechanism has also an important part to play in the regulation of demand for natural gas. For decades, the Federal Government's regulatory agencies have pursued a policy of restricting the prices which can be charged for natural gas to levels at which the utility companies can make a respectable, but not excessive, return on the capital invested in their works. Might it not be better to let prices rise, and to recover at least a part of the extra profit by taxation?

It is also important that the United States Government should make a more hard-headed calculation of the economic cost of some of the environmental measures which have recently been adopted. The regulations now coming into force for the control of exhaust emissions from automobiles are a splendid illustration of how damaging can be over-hasty action in this and similar fields. It now appears—as the more sanguine motor-manufacturers have been predicting, that internal combustion engines designed so as to reduce the output of carbon monoxide and sulphur dioxide to the levels laid down for 1975 will consume an extra 30 or 40 per cent of gasoline. Even the new automobiles manufactured to the 1973 standards are reckoned to need an extra 10 per cent or so of fuel. Given that transportation is responsible for about 60 per cent of petroleum consumption in the United States, this is a splendid way of making sure that the demand for petroleum will increase still more quickly than it has done in recent years. But there are serious doubts about the suitability of the emission standards as a means of ensuring the cleanliness of urban air. The motor manufacturers have a good case when they fear that the catalytic convertors with which new cars will be fitted in 1975 will be as effective as they are supposed to be. There are good reasons for believing that the intended result could in any case be achieved more certainly by a sensible regulation of traffic in city streets. Why impose a serious economic penalty on those who transport themselves in

the outlandish parts of the United States, and at the same time exaggerate the shortage of petroleum, when the real problems are confined to the large cities such as Los Angeles and New York? And in any case, it now appears that the most hopeful way of making clean internal combustion engines is by the more radical redesign of the internal combustion engine to make sure that combustion is more complete. In the past few days, the Environmental Protection Agency has been hearing evidence from the motor manufacturers pleading for an extension of the time required for the imposition of the new standards from 1975 to 1976. If it has the courage, it should respond not by a mere extension of the deadline by one year but by an acknowledgement that the timescale now foreseen is altogether too short, and that it would be more prudent to wait until the 1980s for a radical and more satisfactory solution of the problem of how best to design clean internal combustion engines. To fail to do so will not merely make a nonsense of the earnest but over-pious belief that clean air is a part of the modern heritage, but will also seriously hamper the efforts of the United States to strike an economic balance with its trading partners.

Other conflicts between environmental considerations and the need to keep the world's largest industrial economy in being call for equally fierce action. In this sense, it is a serious scandal that the project to carry petroleum from the North Slope of Alaska to the metropolitan United States should have hung fire for the best part of three years, as much because the United States Government has run away from a decision between the conflicting demands of the environmentalists and the power consumers as for any other reason. Yet the simple question is whether the United States will eventually manage without Alaskan petroleum or accept the environmental nuisance which a pipeline would bring. To postpone a decision, apparently in the hope that a solution to the conflict will eventually emerge, is a recipe for making sure that the petroleum, if it ever starts to flow, will arrive too late. But there are other fields in which a more courageous policy by the government could help to ease the immediate shortage of energy. The siting of nuclear power stations is one obvious field where a sense of resolution by the government could help enormously to take the edge of impending problems. So is the strip-mining of coal in the Western states. On all these local issues, it is entirely proper that the Administration should take account more zealously than in the past of the environmental case against thoughtless development, but who else but the Administration can strike a proper balance between the needs of industry and environmental considerations?

By means like this, there is every prospect that the immediate problems of energy scarcity could be brought within control in the measurable future. Fuller use of the price mechanism and more resolute decision-making by the Federal Government are urgently necessary, but could make the immediate "crisis" go away. By the 1990s, however, the United States will have more serious problems to contend with. It now seems clear that the annual import bill for petroleum products is bound to increase steadily, and the chances are that even by 1980, the United States will be spending $20,000 million a year (or more if there are further devaluations of the dollar) on imported crude petroleum. Numerically, this expenditure is not insupportable, but there are political snags. The Administration is, for example, alarmed at the prospect that so much cash will find its way into the hands

of Arab states which have no automatic sympathy with United States policy in the Middle East — rather the reverse — and which could use their holdings of large quantities of dollars as a way of manipulating the international currency market. But even this is not an entirely unwelcome prospect, for at the very least it will create a climate in which some lasting political settlement in the Middle East will seem to everybody desirable. And here, luckily, there is plenty of time in which the United States can prepare the ground for a lasting policy. To be sure, in the meantime it will be prudent also to pursue as vigorously as possible the technical means by which other sources of energy might be exploited, and no doubt there is much to be done to make use of geothermal steam and solar energy. But the problem of the 1990s is already definable and is largely political in character. It is to be hoped that the United States will not let that blow up into a crisis for lack of resolution in the next few years.

100 Years Ago

SCIENCE AND THE PRESS IN AMERICA
(FROM A NEW YORK CORRESPONDENT)

THE visit of Prof. Tyndall has given an extraordinary impulse to scientific affairs in this country. It took place at a fortunate moment, just after the heat and turmoil of a presidential election had been transformed into the national sorrow over the death of the defeated candidate ; just before the exposures of corruption, which have since disgraced eminent public men, had begun to absorb popular attention. It therefore happened not only that men's minds were not preoccupied, but that, in addition, newspaper columns were not specially crowded. Hence all the leading newspapers gave more space than would have otherwise been possible, to reports of Prof. Tyndall's lectures. In this particular, however, one paper surpassed the rest, giving the lectures verbatim and with illustrations, and afterwards reprinting them in a separate sheet, which, as you are probably already informed, attained a special circulation outside that of the newspaper, of more than 200,000 copies. It is not improbable that this enterprise on the part of the *New York Tribune* originated in a programme for the management of that paper laid down by the late Mr. Greeley. This was printed in its columns the second day after the election, when he resumed his position as editor of the paper. The card specified among other things, first, that thereafter the paper would be enabled to give " a wider and steadier regard to the progress of science, industry, and the useful arts." His successors in the management of the paper have been anxious, for obvious reasons, that it should tread the path he had marked out for it ; Tyndall's coming furnished the first opportunity. Other papers have been stimulated by the popularity of scientific topics, which the success of these lectures revealed, and there never was a time when such themes found such general acceptance with the newspaper press.

From Nature, **7**, 445, *April* 10, 1873

OLD WORLD

Sir Frederick Dainton to be Chairman of the UGC

SIR FREDERICK DAINTON, Dr Lees Professor of Chemistry at the University of Oxford and chairman of the Advisory Board of the Research Councils (ABRC) is to succeed Sir Kenneth Berrill as chairman of the University Grants Committee later this year.

As forecast in last week's *Nature*, Sir Kenneth is to succeed Sir Donald Mac-Dougall as the government's Chief Economic Adviser, but the announcement of Sir Frederick's appointment comes as a complete surprise.

Sir Frederick has played a part in government science for several years and before he was appointed chairman of the ABRC on its inception last year he was chairman of the now defunct Council for Scientific Policy. But Sir Frederick is not cutting himself off entirely from the ABRC for his new position entitles him to a seat on that council. The University of Oxford, however, will be that much poorer for Sir Frederick is resigning his position as Dr Lees Professor of Chemistry.

The decision to leave academic life, said Sir Frederick this week, was one of the hardest that he has had to make. He will miss working with young people and he will miss as well teaching and

research. But Sir Frederick is adamant that he will still keep an active interest in science.

The Advisory Board for the Research Councils, which has now been at work since the autumn, has proved to be more successful than Sir Frederick had at first hoped. It has been a successful forum for the government departments to air their thoughts about research and as a result a great deal of mutual confidence has been built up between the research councils and the departments.

Commenting on the recent government white paper which will change the balance of arts and science students in British universities in the next five years in favour of the arts side, Sir Frederick said that he is concerned that well qualified non-scientists are unable to secure places in universities. In many cases the

qualifications of these art students are better than those of the science students who do manage to get a place. But the white paper will do much to remove this inequity.

Looking to the future and the consequences of a differing rate of growth of the student population and the science budget in the coming years, Sir Frederick said that he is not completely adverse to the concept of university lecturers who do not research. But such lecturers, said Sir Frederick "should breathe the air of a good research department". Sir Frederick also said that it is a bad thing to make a good teacher, who is a reluctant researcher, actually do research. By the same token a good researcher who has no interest in teaching should not be forced to teach.

Pay System Reveiw

THE government agreed late last week to refer the question of scientists' pay within the Civil Service to an independent review by the recently set up Pay Board. This review will take place in the second part of the year.

The government has also agreed that it will be the long term basis of determining scientists pay that will be under review and this will not be influenced solely by short term economic considerations.

Both the official side and the Institution of Professional Civil Servants will be bound by the Pay Board's decision. The IPCS has been demanding an alternative to the current pay research system for eighteen months, but, until now, the government has failed to agree to an independent review. Under pay research the salaries of scientists working in the Civil Service is decided by comparison with the pay of scientists in industry.

ECLIPSE

Science with Concorde

THE Science Research Council is to provide £40,000 for the support of experiments to study the total eclipse of the sun which will be observed from North Africa on June 30.

There will be two sets of experiments. The first, consisting of five or six experiments, will be carried out by British, French and United States scientists on board Concorde 001, while the second, which will be a collaborative venture with scientists from the United States and Canada will be on an Aerobee rocket which will be supplied by the Kitt Peak National Observatory in Arizona.

The British experiments aboard the Concorde will be prepared by scientists from the University of Aberdeen and Queen Mary College, University of London. The British contribution to the experiments aboard the Aerobee rocket will come from the Astrophysics Research Division of the Science Research Council's Radio and Space Research Station and Imperial College, University of London.

The Concorde flight will start from Las Palmas in the Canary Islands and will join the path of the eclipse in Mauritania in West Africa at 10.45 a.m. Greenwich Mean Time on June 30. It will follow the eclipse for almost an hour and a half covering 1,900 miles in that time. This will extend the possible observing time to eleven times that which

will be possible for ground based observers. It is planned that the aircraft will fly at 60,000 feet and so will be well above the layers of the atmosphere which absorb infrared radiation. The French contribution to the cost of the flight will be £130,000.

The University of Aberdeen experiment aboard Concorde will be designed to observe, through a side window in the aircraft, radiation from the near infrared region which is emitted from the stratosphere and mesosphere. From these observations, Dr M. Gadsden of Aberdeen and colleagues hope to deduce the decay times of metastable molecular oxygen. Spectra will also be taken from different heights in the atmosphere in order to determine how the decay time varies with height.

The other British experiment aboard Concorde will be operated by Dr J. E. Beckman and colleagues at Queen Mary College, and it will be designed to obtain a spectrum of the chromosphere in the sub-millimeter region. In order to obtain this spectrum a rapid scan Michelson interferometer with a detector cooled by liquid helium will be used.

The British teams will be joined in the Aerobee experiments by teams from York University in Toronto and Harvard College Observatory, while Kitt Peak National Observatory will provide the rocket, launch and recovery operations. The rocket will be launched from a site in Mauritania near Nouadhibou at 10.33 a.m. Greenwich Mean Time on June 30.

ASTRONOMY

Future of the INT

PROFESSOR GEOFFREY BURBIDGE has, once again, publicized his views on the current state of optical astronomy in Britain. In the correspondence columns of *The Times* on Tuesday of this week, Professor Burbidge, writing from the University of California at San Diego, calls for the Isaac Newton Telescope (INT), now situated at Herstmonceux in Sussex, to be "moved to a good site very quickly". He also calls for an optical observatory to be constructed in the Northern Hemisphere as soon as possible.

It is seven months since Professor Burbidge first gave vent to his feelings about the state of optical astronomy in Britain (see *Nature*, **239**, 117 ; 1972). At that time Professor Burbidge's comments were prompted by the resignation of Professor Sir Fred Hoyle from the Plumian Chair of Astronomy and Experimental Philosophy at Cambridge, and his forthright views made many astronomers respond, first in the pages of *Nature* and then earlier this year in the columns of *The Times* (see *Nature*, **242**, 4 ; 1973).

In spite of the fact that there are 1,900 hours of sunshine a year at south coast resorts near the site of the INT, Professor Burbidge claims that this bears no relation to the time during which the telescope can be used. The INT can only be used, says Professor Burbidge, for 600 to 800 hours a year, whereas the telescopes in California, Arizona and Chile can all be used for up to 2,500 hours a year. But even during the time when the INT can be used, says Professor Burbidge, clouds are frequently present so "that some types of astronomical observations are quite impossible". Very faint objects cannot be observed at all so that cosmological investigations are largely ruled out.

Professor Burbidge, however, is fully aware of the implications of his suggestions that the INT be moved abroad and that a new observatory be built in the Northern Hemisphere. The proposal to move the INT which Burbidge claims has the support of "the majority of the astronomers at the Royal Greenwich Observatory, a large proportion of the younger optical astronomers in the United Kingdom and the expatriate British optical astronomers", is being soft pedalled not because of the cost but because of the fear that if the money is allocated to move the telescope then the government might be reluctant to provide a greater sum of money to build an observatory in the Northern Hemisphere.

A spokesman for the Science Research Council said this week that the council did not have any firm figures for the costs involved in moving the INT and that it would be some time before a firm decision is made on whether or not to move the telescope.

Hidden in Professor Burbidge's letter to *The Times* is a plea that the decision on whether to build an observatory in the Northern Hemisphere should not be delayed by discussion of "exotic schemes". Professor Burbidge calls for a conventional telescope to be installed in the proposed Northern Hemisphere observatory and says that suggestions that a very large telescope should be built or that an array of telescopes be installed should be ignored. Such schemes might take a long time to build —as well as being expensive—and "there is a very good chance that the British would then have constructed a second astronomical white elephant".

SELECT COMMITTEE

No Need for a PhD

THE better the qualifications of a scientist the less chance he has of being employed in industry and big business. This was the sobering thought which the Confederation of British Industry shared with the Select Committee on Expenditure in Higher Education this week.

The CBI, although realizing the need for graduates trained in research techniques, claims that there is no room for the true specialist in industry and that MScs and PhDs are out of their depth once they leave the ivory towers of universities.

The CBI also complained that universities absorb their best graduates, spending many thousands of pounds producing scientists only interested in pure research. A few of these remain in the university after obtaining a higher degree, expanding the boundaries of knowledge, but the remainder are left to find employment in a highly competitive economic world for which they are not suitably trained.

This, according to Mr Campbell Adamson, Director General of the CBI, is not in the national interest. "We want the graduates with good first degrees . . . if they still want to become doctors they should return to university after a few years in industry." Another complaint of the CBI is that too much money is spent in "producing geniuses who immediately get bought up by other countries".

A possible solution, the select committee was told, is for a university to choose its postgraduate students not only on academic achievement but also on personal qualities which indicate their ability to be tomorrow's "top men". This selection could even be done by an independant selector who is in touch with the needs of industry.

AGRICULTURE

Optimism for All

from a Correspondent

OPTIMISM was the order of the day at a recent Royal Society meeting on agricultural productivity in the 1980s. Over 200 agricultural scientists and several farmers heard the future of food supplies discussed with none of the gloomy forecasts about soil deterioration or ecological doom given the prominence which is usual at conferences that impinge on the environment.

Speakers dealt mainly with the situation in Britain, but Dr A. H. Boerma of the United Nations Food and Agriculture Organization struck a somewhat discordant note early on by drawing attention to the difficulties facing developing countries with high birth rates in even maintaining their *per capita* food production. Overproduction in North America and Europe is unlikely to solve the global problem which, he said, is chiefly caused by political and sociological factors.

Professor J. Ashton, an economist, predicted that farming would become more specialized and capital-intensive, while Dr F. C. Lindvall of the California Institute of Technology foresaw a great increase of mechanization throughout the world and of the "power applied per unit of land". He also thought that the manufacturers would have to pay increasing attention to the prevention of pollution and erosion, but such problems, he said, are not insuperable.

Several speakers stressed the need to preserve the whole environment, while Lord Walston saw a growing need for the government to take action to preserve the environment for the benefit of the nation.

In discussing methods of increasing agricultural efficiency Dr W. F. Edson of Fisons thought that even more use will be made of chemical pesticides, that these would not damage the environment, and that non-chemical methods of pest control would only make a minor contribution. Dr A. B. Paterson from the Central Veterinary Laboratory, Weybridge, forecast that disease prevention would contribute to increased productivity of all livestock.

Dr N. W. Simmonds of the Scottish Plant Breeding Station argued that plant breeders would continue to produce increased quantity and quality in crops, while Professor A. W. Holmes of the British Food Manufacturing Research Association spoke of substitute foods, mainly proteins from soya beans, producing samples aimed at the high-quality market for the audience to try.

But the most thought-provoking part of the meeting was Sir Joseph Hutchinson's final address which, except for Dr

Boerma's contribution, was the only one to descend from the general level of euphoria. Sir Joseph stressed the dangers of a purely economic approach —a surplus of five per cent at present could mean financial ruin for the producers, he said, while a shortage of a similar amount could mean starvation and death in some areas. The need for a global food store is obvious. He also queried the wisdom of introducing capital-intensive farming to developing countries with the result that an unemployed urban proletariat is created. Labour-intensive techniques might be wiser, he said.

Sir Joseph was the only speaker, apart from Dr Boerma, not convinced that all forecasts would be reached without more knowledge arising from increased research on the soil and its potential, which he described as the "patient Cinderella" of agriculture.

ISRAEL
Political Scientist

DR EPHRAIM KATCHALSKY, the noted Israeli biophysicist, is to become President of Israel next week. Dr Katchalsky, who is head of the department of biophysics at the Weizmann Institute, has been nominated by the Israeli Labour Party as its candidate for president. That means certain election as president on April 10 when the Knesset, the Israeli parliament, meets. He will take office in May.

Dr Katchalsky, who was on a lecture tour of the United States when he heard the news, is well known for his work on the physics of large molecules and membranes. He was the first to synthesize polylysine, a molecule that is much used in immunological research.

The post of president in Israel is largely that of a figurehead and has always been filled by an intellectual rather than a politician.

When he takes office Dr Katchalsky will be the fourth president of the country, his predecessors being Dr Chaim Weizmann, founder of the Weizmann Institute, Mr Itzhak Ben-Zvi and Mr Zalman Shazar, who is now retiring, aged 83, after ten years in office.

Dr Katchalsky was born in Kiev in the Soviet Union in 1916 but moved to Israel when he was a child. He was educated at the Hebrew University in Jerusalem and has held various government posts in Israel, experience that will serve him well.

When the news of his appointment came through Dr Katchalsky was in Berkeley in California attending a three day symposium held in memory of his brother Professor Aharon Katzir Katchalsky who was killed in the Lod airport massacre in May 1972 (see *Nature*, **237**, 304 ; 1972).

COMPUTERS
Wake for Atlas

THE original ICL Atlas I computer at the Science Research Council's Atlas computer laboratory was closed down last week after more than eight years' service. In the closing ceremony Sir Brian Flowers, chairman of the Science Research Council, switched the Atlas off after Professor David Howarth, who wrote the operating system for the computer, had run the last programme.

Atlas's work has now been taken over by an ICL 1906A, which was installed in 1971. This computer is some three times faster than Atlas.

Atlas was designed at the University of Manchester between 1957 and 1961 by a team led by Dr Tom Kilburn. Among the features that made it one of the most advanced machines in the world at the time were a number of facilities that have since become standard such as its permanent master programme and paged store.

The Atlas was ordered in 1961 and installed between 1962 and 1964. For its day it was fast. Simple operations such as addition took about 2 microseconds, and it could solve 100 linear equations in about 10 seconds. Since Atlas was built, however, machines 20 times faster than Atlas have been introduced.

Now that it has been switched off, what is to happen to the computer? The answer is that bits of it will find their way into museums all over the world and the rest will be sold for scrap. Dr J. Howlett, Director of the Atlas Computer Laboratory, said this week that "if some university could install and run it we could probably give it to them" but the problems of moving and maintaining such a large and comparatively ancient machine are enormous. ICL's contract to maintain Atlas expires next year, and finding spares for the machine, if it goes wrong, is likely to be a problem soon. The Atlas Laboratory intends to keep the front end processor with its 100 million character disk, as this is a self-contained unit, and a couple of the Ampex TM2 1 inch tape decks may stay in use although nominally they are obsolete. The Chilton machine is the last but one of the six Atlas computers built to be scrapped. Only the Atlas at the Department of Trade and Industry's computer Art and Design Centre at Cambridge is still running.

During its eight and a half years' operation the Atlas has been available 97 per cent of the time and has handled 836,000 jobs valued at £10.8 million. More than 2,300 university projects have been put onto the computer.

Sir Brian said during the ceremony that the SRC is currently considering the successor to the ICL 1906A. The problem is one of trying to predict the needs of scientists and then finding a machine that will do the job rather than choosing a machine and then seeing what can be done with it.

TRIBOLOGY
Satellites and Friction

TESTS are to begin this week on solar paddles for the European Space Research Organization's communications satellites.

ESRO's Space Tribology Laboratory (ESTL), which is situated within Britain's National Centre of Tribology at Risley in Lancashire, was founded a year ago and in that time six 40 cm ultra high vacuum chambers have been installed in a clean room that is now fully operational. Six slow speed solar paddle drive mechanisms, capable of one revolution every twenty-four hours were due for delivery a few weeks ago and are to be installed this week. Three each of two designs produced by Hawker-Siddeley and Marconi are to be tested and some of the tests will run for seven years—the minimum life of a communications satellite.

The ESTL contract which is worth £400,000 over four years is the largest feather in the National Centre of Tribology's cap, but the centre has been plugging happily away as a contract research organization for five years during which time, apart from the ESRO contract, it has acquired £0.25 million of business. Contracts have ranged from consultancies costing a few hundred pounds to development contracts worth tens of thousands of pounds and the tribological problems the centre has tackled have ranged from making gas bearings to designing window hinges for high rise flats, from pop-up toasters to pulverising plants and artificial heart valves.

The centre's work falls roughly into three equal parts, the ESRO contract, industrial contract work and work on the Atomic Energy Authority's reactor systems. It was the UKAEA's need for moving parts in the hostile environment of reactors where temperatures are high and service is difficult or impossible that led to the centre's formation. Originally part of the materials group at Risley, the centre began to apply commercially the knowledge gained in developing Magnox and AGR reactors.

Now the contract work plays a larger part in the centre's programme than the UKAEA work, but twenty per cent of the centre's efforts still goes into work on the sodium cooled fast reactor.

As the centre has become better known its activities have expanded, and the 5 man team that started work in 1968 is now 30 strong. Turnover next year is expected to top £250,000.

NEW WORLD

Cancer Advisory Board Expresses Concern

by our Washington Correspondent

THE National Cancer Advisory Board, the chief advisory body to the National Cancer Institute, last week sharply criticized the Administration's plans to phase out NIH training grants and fellowships, and appealed directly to President Nixon to get them reinstated. Specifically, the board passed a resolution during its regular quarterly meeting requesting the President's Cancer Panel — a panel consisting of three members which reports directly to the President— to "seek a personal audience with the President" to bring the Board's concern to his attention.

The Administration's budget request for 1974 proposes that NIH training grants should be phased out, and provides no money for approving new grants. Only those grants which still have some time to run will be funded, and so eventually, if the Administration gets its way, the NIH will be forced entirely out of the business of giving direct support to graduate students.

The Administration supports its case by arguing that since research budgets are now "stabilized", demand for manpower will not grow as quickly as it has in the past few years, and there is danger of an oversupply of trained biologists. It has also been argued that since scientists who hold a PhD expect to earn large salaries, they should be able to finance their training by taking loans.

But the Administration's plans have been attacked vehemently by university scientists, who have complained that phasing out the training grants will choke off the supply of graduate students. Dr James Watson, Professor of Molecular Biology at Harvard and Director of the Cold Spring Harbor Laboratory, recently told the Senate Health Subcommittee, for example, that the policy is "lunacy". He pointed out that most important new discoveries in biology come from people under the age of 35 who are relatively unknown at the time they make their breakthrough, and so the shutting off of NIH training grants and fellowships, coupled with the trend towards contract research, will concentrate resources in the hands of middle aged entrepreneurs. Also the science will for the most part have to be done "by an age group not noted for working into the night".

Watson's statements to the Senate Health Subcommittee were also backed by Dr Lewis Thomas, Dean of Yale University School of Medicine and President-elect of the Memorial Sloan Kettering Cancer Center. Both Watson and Thomas are, however, university scientists who represent the group most severely affected by the cutbacks. They could, therefore, be accused of special pleading. But earlier this week, the Carnegie Commission on Higher Education, in a report on the job outlook for graduates, reported that prospects are bright for graduates entering the health care professions, and also warned against any cutbacks in federal funds for training in health and allied professions.

CONGRESS

New Force in the Senate

by our Washington Correspondent

WHILE the Administration has been scrapping, revamping and—some say—downgrading its science policy machinery, Congress has been quietly building up its scientific strength. The latest move is the setting up of a subcommittee on Science, Technology and Commerce as part of the Senate Commerce Committee. Although the subcommittee's role is still being worked out, it has a broad mandate to study scientific and technological questions, and it seems that its work will to some extent parallel that of John Davis's subcommittee on Science, Research and Development in the House of Representatives.

The chairman of the new subcommittee is Senator John Tunney of California, and other members so far appointed are Adlai Stevenson III of Illinois and James Pearson from Kansas. Both Tunney and Stevenson were appointed to the Commerce Committee for the first time this year. It will be the first subcommittee in the Senate to have such a wide-ranging interest in science since the demise in 1969 of Senator Fred Harris's subcommittee on government research.

One of the subcommittee's chief concerns will be the workings of the National Bureau of Standards, which is part of the Department of Commerce, and in that respect it will handle all the legislation dealing with metric conversion. Fire safety research and development will also fall in the committee's purview. But Senator Warren G. Magnuson, chairman of the Commerce Committee, clearly sees the subcommittee as having a broader role than simply overseeing the affairs of the NBS, for he said last week that it would be concerned with the "taming and channel-

Started in 1946, the NIH training and fellowship programmes grew steadily until last year, when the funding reached nearly $190 million. This year, funding is being held at $150 million, and it is set to go down next year to $129 million. Moreover, general research support for every institute except the National Cancer Institute and the National Heart and Lung institute is also set to decline, which in turn will mean that there will be less money available in the universities to support graduate students from the general project support grants.

ling of technology towards the solution of national problems". An aide to Senator Tunney added that the subcommittee will also probably take a close look at investment in science and technology in relation to the US balance of payments.

An important factor is that Senator Tunney is a close personal and political friend of Senator Edward M. Kennedy, and cooperation between his subcommittee and Kennedy's subcommittee, which oversees the work of the National Science Foundation, is therefore to be expected. Such cooperation would, for example, facilitate any move to broaden Kennedy's National Science Policy and Priorities Act (S32) to provide a role for the National Bureau of Standards. In the House of Representatives, such jurisdictional problems would not arise because Davis's subcommittee has oversight over both the NSF and the National Bureau of Standards.

Congress's other new science unit, the Office of Technology Assessment, is still waiting for funds before it can officially get under way. A supplemental appropriations bill is not now expected to be passed until June or July at the earliest, and so appointment of staff and the initiation of studies will have to wait until the summer or autumn. There has also been a minor squabble among the members of the OTA board of directors appointed from the House of Representatives, about who should be the board's vice-chairman. Kennedy has already been elected chairman, and John Davis reckons that he should get the job of vice-chairman. But Charles Mosher, a Republican from Ohio and ranking minority member on Davis's subcommittee, reckons the job should go to a Republican, namely himself. And that is where the matter stood last week. The OTA board meets for the first time next week, and the office's advisory council may then be appointed.

The Administration argued when it phased out graduate support grants from the National Science Foundation that graduate students would be able to pick up their support from project grants, and it has also applied the same argument to the NIH training grants. But the National Cancer Advisory Board looks on that argument with considerable scepticism, for although its recommendation that training grants be reinstated in theory applies only to the National Cancer Institute, several board members are particularly concerned about the effect on the cancer programme of cutbacks in other biomedical sciences.

The resolution adopted last week specifically points out that the National Cancer Act of 1971 specifies that the board, together with the director of the National Cancer Institute, should provide a sufficient manpower base in fundamental sciences and clinical disciplines to carry out the cancer program. "The Board feels that it cannot carry out those responsibilities in the absence of authority to fund training programs", the resolution states.

If the board's appeal falls on deaf ears in the White House, which seems likely, it is unlikely to go unheeded in Congress —Kennedy, for one, will probably try to get the training programs reinstated. But, if the history of the National Science Foundation's graduate training programmes is anything to go by, the Administration will get its way in the end. For the past three years, Congress has directed the Administration to increase its proposed spending on NSF graduate support grants, but each year the Office of Management and Budget has simply impounded the extra money.

AIR POLLUTION
Reducing Hazards

by our Washington Correspondent

THE Environmental Protection Agency has at last set controls on the discharge of asbestos, beryllium and mercury into the atmosphere. Designed to protect public health, the controls apply to milling and manufacturing industries, the demolition of buildings and the burning of wastes. They have taken more than two years to develop—a year longer than the Clean Air Act allows—and the EPA reckons that they will cost industry a little more than $50 million a year, with the chief cost falling on the demolition industry.

The three pollutants were chosen because they each have a potentially serious impact on public health, causing or at least contributing to increase in mortality, and serious and incapacitating illness. But, although the need for stringent control over their emission has been widely recognized, the EPA has had

considerable difficulty in drawing up suitable regulations.

As for asbestos, it is extremely ubiquitous, tiny asbestos fibres in the atmosphere constitute a serious health problem, and it is very difficult to regulate. The fibres lodge in the lung, causing a debilitating and often fatal condition among asbestos workers, known as asbestosis. They have also been linked with cancer of the lung and with a variety of other cancers. A widely publicized study by Dr Irving Selikoff of the Mount Sinai Medical School, for example, has come up with the prediction that about 95,000 of the estimated 250,000 asbestos workers in the United States will eventually die of cancer.

Such considerations led a committee of the National Academy of Sciences to recommend last year that stringent controls should be placed on the emission of asbestos fibres into the atmosphere, but the setting of such controls has been hampered by the fact that satisfactory means of measuring ambient asbestos concentrations have only recently been developed, and a method of measuring asbestos emissions is still unavailable. The EPA even considered banning production, processing and use of asbestos completely, but eventually decided that such a drastic step would lead to the banning of extremely important uses of the material.

In the event, the agency decided to set visible emissions standards for a number of operations, and to require that a specific procedure be followed in the demolition of buildings. In short, the regulations set last week specify that there shall be no visible emission of asbestos from asbestos mills or from the manufacture of any product which contains asbestos, such as cloth, floor tiles and insulating materials.

As for demolition of buildings containing asbestos products, the regulations specify that the material should be removed before the building is demolished, that it should be wetted before removal, and that the EPA should be notified at least 20 days before demolition takes place. The regulations apply to all buildings except homes and apartment buildings with four living units or less. The controls are expected to increase demolition costs by about 8 per cent.

The beryllium and mercury standards were a little easier to draw up, because emission of each pollutant can be measured. The beryllium regulations apply chiefly to extraction plants, foundries and ceramic manufacturing plants and they specify that the maximum daily release of beryllium into the atmosphere from a plant should be 10 grams. As for mercury, the regulations specify that no more than 2,300 grams of mercury vapour should be released from stationary sources.

BALLOON RESEARCH
Long Life Aloft

by our Washington Correspondent

AFTER making two complete orbits around the Earth in 36 days, an experimental balloon carrying about 90 pounds of scientific instruments was brought back to the ground within 10 miles of its launching site in Australia last month. A second balloon, launched at the end of January, is still aloft after being becalmed over the South Pacific, and it is expected to complete its second orbit later this month. The flights, which were carried out as part of NASA's balloon research programme, represent the first succesful orbiting of scientific instruments by balloon, and they are an important step on the way to development of a balloon capable of orbiting up to about 500 pounds of instruments at 130,000 feet, and of staying aloft for six months or more.

Although the balloons carried scientific instruments—cosmic ray detectors and micrometeorite collectors—the chief objective of the flights was to test the performance of a new type of balloon. Called super pressure balloons, they are designed to fly at an altitude determined by constant atmospheric density, and unlike conventional balloons, they have no valve for venting gas when excess pressure builds up. Consequently, the skin must withstand changes in pressure caused by temperature changes between night and day, and it must also be resistant to degradation by ultraviolet light and fast moving micrometeorite particles.

Conventional balloons are usually inflated on the ground and lift the payload to the required height. As the altitude increases, the balloon expands and excess pressure is vented from a valve at the base, but at night, when the temperature drops, the balloon shrinks and descends. The skin is, however, not completely elastic, and when the balloon expands again during the day, it vents some more gas. Consequently, conventional balloon flights provide only a few hours worth of scientific results.

Super pressure balloons, on the other hand, are constructed of material which can withstand the excess pressure developed by changes in temperature, and they are also designed to be resistant to degradation by strong ultraviolet light and fast moving dust particles in the upper atmosphere. The two balloons which NASA has been orbiting will now be carefully studied for signs of wear, and if they have survived their flight successfully, the prospects for lifting payloads to 130,000 feet for several months seem very good.

If NASA's objective is attained, super pressure balloons would open up considerable new possibilities for upper

atmospheric studies and for cosmic ray research. Although even at that height, atmospheric effects would interfere with X-ray and gamma-ray astronomy, Dr Carl Fichtel of NASA's Goddard Space-flight Center, said last week that long and reliable balloon flights could be "extremely valuable" for low flux events, such as high energy electron-positron studies.

As for the two test flights, the balloons were carried to a height of about 78,000 feet by a small conventional balloon, and then released. They were carried by the air stream in an orbit passing over Australia, Africa and South America. The original intention was to bring the first balloon down after one orbit, but weather conditions at the landing site were not good, and it was decided to leave it to make another orbit. And, now that the second balloon has become becalmed, NASA will be able to look at the effects on the skin of at least 60 days exposure to intense ultraviolet radiation and micrometeorites.

PESTICIDES

Firing the Ant

by our Washington Correspondent

THE Department of Agriculture's long war against the imported fire ant — an insect with a painful sting which has established itself in the Southern United States—will move to a new battleground this summer. The Environmental Protection Agency has called a number of public hearings to help it decide whether a controversial pesticide known as Mirex should continue to be used against the ant. The hearings may finally put an end to the considerable controversy which has surrounded the Department of Agriculture's campaign against the ant in general, and the use of Mirex in particular, and a decision will be made before August 15, when the autumn treatment programme is due to begin.

First introduced into the United States from South America in the 1920s, the fire ant has since spread through the south-eastern states, from Texas to North Carolina. Although it does little or no direct damage to crops, the ant has been treated to an onslaught of pesticides in campaigns financed partly by the US Department of Agriculture (USDA) because of its painful sting and because its mounds damage agricultural machinery. The USDA programme at first attempted to eradicate the ant, but recently has concentrated on trying to prevent it from spreading any further.

The campaign against the ant has, however, been attacked by environmentalist groups and by several scientists, partly on the grounds that it is not worth the expense, but also because the chief weapon, Mirex, persists in the environment, tends to collect in some

animals and insects and has been found to cause cancer in mice. In March, 1971, William D. Ruckelshaus, Administrator of the Environmental Protection Agency, decided to cancel registration of Mirex because of the doubts about its safety, but the chief manufacturer, Allied Chemical Corporation appealed the decision and asked for review of the pesticide by an independent scientific advisory committee. The committee eventually gave qualified approval to Mirex, and in July last year, Ruckelshaus lifted the cancellation order but forbade use of the pesticide near water or heavily forested areas, and also stopped application from aircraft in coastal regions. The hearings this summer will re-examine those decisions.

The scientific advisory committee which examined the use of Mirex last year (see *Nature*, 235, 353 ; 1972), concluded that the ant should be controlled because its presence restricts use of recreational areas, and because it is continuing to spread. The committee also concluded that Mirex is effective in controlling the ant, that it is not acutely toxic to man, and that it does not seem to present much of a long term hazard although more chronic toxicity studies are urgently needed. Mirex residues have, however, been found in relatively high concentrations in aquatic animals, and the committee consequently recommended that it should be kept away from water.

The pesticide is applied in small doses in a bait which the fire ant takes back to the mound, and it then wipes out the whole ant colony. When the Mirex treatment campaign first started about 15 years ago, the Department of Agriculture pumped more and more money into it, and was egged on by Congressional agriculture committees. But as the ant continued to spread, it became clear that complete eradication was impossible, and the USDA has recently been concentrating on preventing the ant from spreading. This year the USDA intends to treat about 20 million acres out of a total infested area of about 126 million.

Short Notes

Lunar Studies

THE National Aeronautics and Space Administration has announced that it has established a new programme for analysing lunar data derived from the Apollo programme. Called the Lunar Data Analysis and Synthesis Program, it will encourage multidisciplinary studies which draw on data from a number of sources, such as Apollo experiments and photography, lunar mapping, Moon samples and theoretical studies and Earth-based observations. The lunar programme is now part of the Office of

Space Science, and the Lunar Programs Division is headed by William T. O'Bryant.

Second Biggest

KITT Peak National Observatory, atop a sacred mountain of the American Indians of southern Arizona, will soon have the second largest telescope in the world. The 158-inch Mayall Telescope, named after a director of the observatory, is now undergoing final tests before observations start in October.
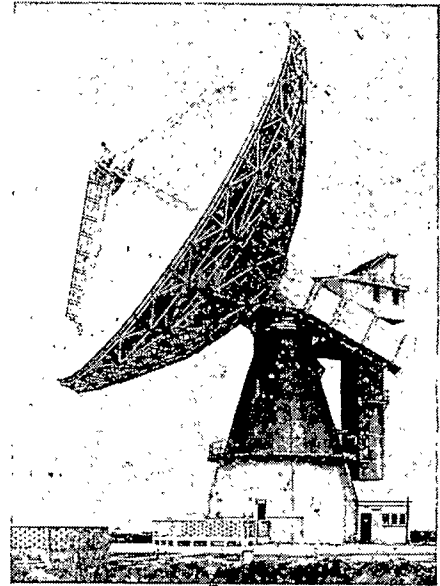
Financed at a cost of $10 million by the National Science Foundation, the telescope is housed in this building designed by the Chicago office of the Skidmore, Owings and Merrill architectural firm which also designed the visually striking McMath Solar Telescope also on Kitt Peak.

Weather Modification

A RESOLUTION was introduced into the House of Representatives last week by Mr Don Fraser of Minnesota calling on the United States to seek agreement with other members of the United Nations on a treaty banning "research, experimentation or use of weather modification activity as a weapon of war". A similar resolution was earlier introduced into the Senate by Senator Pell.

Psychosurgery

A TWO-YEAR moratorium on federal projects involving psychosurgery was called for last week by three Republican Senators. Senators Beall of Maryland, Dominick of Colorado and Buckley of New York introduced a bill into the Senate calling for such a moratorium and also directing the Secretary of Health, Education and Welfare to conduct a comprehensive study of psychosurgery and to recommend within a year, what circumstances, if any, justify its use.

NEWS AND VIEWS

Record QSO Redshift Observed

ALMOST exactly ten years ago, on March 16, 1963, the story of quasistellar objects (QSOs) began in the pages of *Nature* (**197**, 1037) with the announcement of the identification of the radio source 3C 273 with a thirteenth magnitude stellar object with a redshift (z) of 0.158. Anybody following, even casually, this continuing story must by now be acquainted with some of their chief features. QSOs are now recognized as being associated with about 25 per cent of the known radio sources. Using direct photography most of those so far identified are difficult to distinguish from normal galactic blue stars although they differ from such stars in having a characteristic ultraviolet excess; that is, they not only appear brighter on the blue O-plate of the Palomar Sky Survey than on the red E-plate but also appear brighter on a plate taken with an ultraviolet (U) filter than would a galactic star which appears equally bright using a blue (B) filter. A conclusive identification, however, requires a spectroscopic analysis to show the characteristic broad emission lines (among them and typically the strongest Lyman α, CIV, CIII, MgII and Hα) which are shifted towards the red by an amount greatly in excess of that observed in extragalactic nebulae of comparable apparent magnitude.

Immediately following the discovery of QSOs it was realized that on the conventional interpretation of the redshift in terms of the Doppler effect associated with the expansion of the Universe and related to distance by Hubble's law, QSOs provided the most powerful tool available for the investigation of the geometry and history of the Universe. Using even the brightest radio galaxies it was clear that optical observations could be extended to redshifts greater than 0.5 only with great difficulty, whereas with QSOs such investigations could be contemplated for objects with $z \geqslant 2$ where the differences between various cosmological models becomes large. With the cosmological problem in mind strenuous efforts were therefore made to detect more and more QSOs, particularly QSOs with large redshifts. These searches were carried out in two ways: optically, using U and B filters first to detect objects with the characteristic ultraviolet excess, and by using lists of radio positions to locate blue stellar objects on the Palomar Sky Survey plates (radio positions were in general not sufficiently accurate to permit a reliable identification on the basis of positional agreement alone). Progress was at first rapid and by 1966 some 100 redshifts, some as large as $z \simeq 2.2$, had been measured. Since then progress has been significantly slower and only two or three objects with larger values have been reported, the record ($z = 2.877$) being held by an eighteenth magnitude QSO associated with the radio source 4C 05.34 (Lynds and Wills, *Nature*, **226**, 532; 1970). As this QSO is well above the magnitude limit of the Sky Survey plates and noticeably blue, Lynds and Wills considered that there could be no significant selection effects preventing the discovery of such objects up to $z = 3$ and therefore that the low rate of discovery of objects with high redshifts must be a consequence of their intrinsic rarity. An essentially similar conclusion has been reached by Schmidt (*Astrophys. J.*,

176, 273; 1972) who analysed an optically selected sample of QSOs and found that the distribution of redshifts could only be explained if the density of QSOs (per unit of comoving volume) increases approximately as $(1+z)^6$ up to a redshift of approximately 2, but then decreases, or at least increases much less rapidly.

This conclusion raises the interesting possibility that a redshift of 2 represents an important epoch in the evolution of the Universe but is somewhat disappointing in that it indicates a degree of density evolution that is certainly sufficient to mask the geometrical effects expected from different model universes. If this is indeed the case it may still be possible to distinguish between different cosmologies using a method first suggested by Hoyle, who pointed out that in most cosmological models a source of given linear size reaches a minimum apparent angular size at $z \simeq 1$, beyond which the apparent size for various models rapidly diverges. No such minimum has yet been detected but here again evolutionary effects may be important and it may be necessary to go to redshifts greatly in excess of 2 before the geometrical effects become apparent.

Cosmologists will therefore be elated by the report from Carswell and Strittmatter on page 394 of this issue of *Nature* that the barrier at $z = 3$ has at last been crashed. Of particular interest is the fact that it has been observed on the basis of positional agreement alone and without the help of the usual selection criteria, thus raising the question whether, up to now, these selection criteria have been militating against the detection of high redshifts.

It has long been known that at least the magnitude of the ultraviolet excess is dependent on redshift (Strittmatter and Burbidge, *Astrophys. J.*, **147**, 13; 1970), largely as a result of the passage of the strong emission lines through the relatively narrow U filter. In particular there is little doubt that the ease with which redshifts around 2 have been measured is attributable to the shift of the strong Lyman α at this redshift from its rest wavelength of 1,216 Å to 3,648 Å, near the peak response of the U filter. For a redshift range $z = 2.2$ to 3, however, Lyman α appears instead in the B filter with the result that the ultraviolet excess may disappear although the object may still appear blue. Browne and McEwan (*Nature*, **239**, 101; 1972) have noted a number of objects which have these characteristics. The sharp decrease in the continuum at wavelengths shorter than 4,000 Å noted by Carswell and Strittmatter certainly shows that QSOs with $z > 3.4$ will not be characterized by an ultraviolet excess. This is not to say that high redshifts may not indeed be rare, simply that they will be difficult to detect by optical search techniques. It would seem that a significant extension of the observations to redshifts greatly in excess of 3 will therefore be difficult on account of the lack of an ultraviolet excess.

Positions accurate to about 1 arc s will be required, for it is clear from the identification of OH 471 that the usual blue criterion will not be applicable. Indeed it may be worthwhile to reverse this criterion and concentrate on very red objects. Thus a QSO with a redshift of $z \simeq 4$ will have Lyman α shifted to the peak response of the

E-plate and with the form of the continuum spectrum described by Carswell and Strittmatter may appear very red indeed. Furthermore Lyman α is so strong relative to the continuum that its presence may more than compensate for the increase in distance so that a QSO with $z \simeq 4$ may be even brighter than the eighteenth magnitude object associated with OH 471. The detection of objects with even higher redshifts is clearly feasible particularly if plates are used with a peak response significantly to the red of the Palomar E-plate.

The observation of Carswell and Strittmatter thus holds out hope that with radio positions accurate to 1 arc s becoming routinely available, objects will be identified with sufficiently high redshifts to allow a separation of the geometrical effects of different cosmologies from evolutionary effects. They have shown that although these high redshift objects may be rare they do exist.   C. H.

Marine Conservation

SUCH has been the success of marine conservation areas in the several countries which have set aside sublittoral areas for total protection or controlled exploitation, that it was inevitable that pressure would mount for a conservation policy for marine habitats in the British Isles. A working party on marine wildlife conservation set up by the Natural Environment Research Council has recently produced an assessment of evidence of the threat to marine wildlife and the need for conservation measures (*Marine Wildlife Conservation*, NERC Publ. Series B, No. 5, 39 pp ; 1973). The working party, under Professor R. B. Clarke, reports that some 461,000 acres of coastal habitat —consisting of mud flats, marsh, cliffs, sand dunes and shingle—are already conserved within National Nature Reserves, but that most of these exist not because of their littoral importance but because they have ornithological or physiographical interest. A substantial area of marine habitat is thus already partly protected more by accident than design, a phenomenon attributable to the terrestrial base of the Nature Conservancy.

One of the priorities of the working party was to establish exactly what changes had taken place in the marine flora and fauna and the factors involved in the changes ; a substantial part of the report is concerned with this evidence. A second priority was to examine the current marine conservation measures in the United Kingdom. Recommendations for action should clearly stem from both.

The difficulty in practise is that recommendations can only stem from a position of knowledge, and it seems from the evidence presented that the facts concerning change in status of marine organisms are acutely inadequate. Even the report enters the caveat "that the evidence we received was largely circumstantial, relates to comparatively few areas, and came from relatively few sources". Evidence of changes were received from members of staff of marine laboratories and fisheries departments, local authorities, sea fishery committees, conservation societies and other interested organizations. Given the necessity of gathering information by questionnaire, the variety of interest here could be sure to reveal some bonnets buzzing loudly with bees.

Analysis of the evidence presented, in which changes of abundance are related to the causative factor, produces an interesting league table:

Skin Divers	26	Climatic change	14
Pollution	9	Bait digging	9
Unknown	21	Others	2

Skin divers are thus clear favourites. Most of the reported consequences of their activities refer to local exploitation of stocks of commercial shellfish—crabs, lobsters, crawfish especially, and scallops. Heavy collecting of the sea fan, *Eunicella* and the sea urchin, *Echinus*, for sale to tourists in the major holiday resorts, is also reported. The coasts of Dorset, Cornwall, the Isles of Scilly and West Wales are particularly affected, but this is because these areas are suitable for diving. Many other areas contain these species in abundance, but because of inaccessibility, or cloudy water, are unsuitable for diving which suggests that over exploitation will never be more than a local phenomenon.

Bait digging in intertidal areas is an unexpected hazard to the marine biota but is certainly over-emphasized in the analysis. In fact, eight out of the nine cases of reported decline are concerned with marine worms and most of these reports stem from a single observer and locality. As the working party's report points out, disturbance of the foreshore by bait digging may expose other invertebrates and lead to their decline —but no evidence is produced to quantify this effect. Moreover only four widely distributed areas are named where damage from bait digging is reported.

Decline in numbers as a result of pollution is also reported, especially among molluscs, filter feeders and algae in heavily polluted areas such as the Mersey mouth and the Durham coast. Sea anglers too are said to have had reduced success in the Bristol Channel, Solent and Weymouth areas, a report "which is authenticated by club records". "Authenticated" might seem a strong word for evidence from angling club records. Most anglers attribute their lack of success to factors beyond their control, and "pollution" is a convenient and fashionable whipping boy.

Two other principal causes of change in the marine fauna are "unknown" (records for which mostly stem from professional marine biologists) and climatic changes (which have been for long well documented in the scientific literature).

These examples are symptomatic of much of the evidence showing that the marine fauna and flora has changed appreciably in the recent past. In essence they suggest that the most important factor causing changes in the marine environment is climatic, which has long been appreciated and studied. The remaining evidence may suggest local trends which require quantitative assessment but more likely to be attributable to the totally subjective nature of much of the evidence.

The working party's recommendations to NERC, that in view of the paucity of factual information long-term studies into natural population fluctuations be intensified and that sources of information and advice should be identified and involved in future conservation measures, are clearly unavoidable and highly desirable. The setting aside of littoral and sublittoral areas as conservation reserves equally clearly can wait until the need for them is established by quantitative evidence gathered by objective survey.

From a Correspondent

FOETAL PHARMACOLOGY

Drugs and the Unborn Child

by our Special Correspondent

SOME pregnant women are probably consuming drugs unnecessarily, to the detriment of their future offspring. This warning from several speakers at a symposium in New York on March 15 and 16 was underlined by the revelation of general ignorance of many of the effects of drugs on the human foetus. The occasion was a gathering of representatives of all disciplines associated with human development, brought together by the March of Dimes to discuss recent advances and unsolved problems concerning drugs and the unborn child. As the meeting progressed, however, unsolved problems predominated the proceedings, and it became clear that it is by no means simple to identify a particular drug as a potential hazard to the foetus.

The voracity of pregnant women for drugs is well illustrated by a retrospective study of 911 women in Edinburgh, reported by Dr J. O. Forfar (University of Edinburgh). His team found that, excluding iron, drugs were prescribed for 82 per cent of the women during pregnancy, with an average of four drugs each. Sixty-five per cent of the women took non-prescription drugs, mostly aspirin and antacids. The survey revealed a tendency to administer certain drugs—antibiotics, cough medicine, iron and tranquillizers—throughout pregnancy; others—antiemetics, antihistamines, appetite suppressants, bronchodilators and hormones—early in pregnancy; and others —for example, antacids, analgesics, barbiturates, diuretics and hypnotics—late in pregnancy. Dr Forfar's conclusion that the basis on which many of these drugs were used could be questioned, was echoed by Dr L. Stern (McGill University). He wondered whether, for example, all the pregnant women who took thalidomide, and later gave birth to severely malformed babies, had really needed the drug as treatment for insomnia.

Other speakers urged great care in the prescribing of drugs during pregnancy. But the situation for the physician is often not clear cut, as was explained by Dr L. M. Hellman (US Department of Health, Education and Welfare). The value of a drug must be measured according to the ratio of benefit to safety, which makes it very difficult for anybody to rule that a particular drug should never be given to pregnant women. For example, some attention at the symposium focused on diphenylhydantoin ('Dilantin'), which is suspected sometimes to cause birth defects such as cleft palate. But 'Dilantin' is an important anti-convulsant drug, which is given to pregnant women as a treatment for epilepsy. As epileptic seizures must obviously be avoided during pregnancy it would be rash immediately to ban or restrict the use of this drug.

Faced with such problems, the physicians turn for information to the experimentalists, who are beset with problems of their own. The effects of drugs on the foetus can only be assessed in comparison with the normal sequence of changes involved in biochemical development. At present little is known about the situation in the human foetus, and so it was not surprising that contributors to the biochemical sessions of the meeting concentrated on reviewing data obtained with rodents and other animals. Dr O. Greengard (Harvard University), for example, reported progress with the rat, revealing that four different groups of enzymes, induced by various hormones, appear at four different stages of foetal development. Unfortunately, as data slowly amass, it becomes increasingly clear that the human foetus, far from resembling the rat, is biochemically unique in its development. Dr D. B. Villee (Harvard University) reported that the biosynthetic pathway of the steroid hormones in the human develops quite differently from that in other species. This underlines one of the greatest problems of students of drug metabolism—the paucity of suitable animal models that can be trusted to parallel the situation in the human foetus. The baboon, however, offers some hope as a model for the study of foetal steroid metabolism, according to Dr S. Solomon (McGill University).

Summarizing the many goals of developmental pharmacologists, Dr B. L. Mirkin (University of Minnesota) gave highest priority to the study of the passage of drugs into the foetal environment throughout gestation; the effects of drugs on normal development; the influence of postnatal maturation on drug disposition; and inherited and acquired factors influencing the action of drugs. Increased

A Common Receptor for Hallucinogens?

IT is always the hope that elucidating the mechanisms of hallucinogenic drugs will give clues as to the nature of mental disorders and ways of developing treatment. Psychopharmacologists would no doubt be delighted to find that hallucinogens operate by way of a common effect.

Szent-György's group have studied several psychoactive compounds and suggested that their action might result from their powerful ability to donate electrons (Science, 130, 1191; 1960). Snyder and his co-workers have found a high correlation between the potency of hallucinogens and their willingness to give up electrons (Proc. US Nat. Acad. Sci., 54, 258; 1965). Three dissimilar classes of drugs have been found to produce psychedelic effects—lysergic acid diethylamide (LSD), derivatives of tryptamine, and compounds related to phenylethylamine. Theoretical calculations showed that within each class, the agents which can best donate electrons are those with the greatest hallucinogenic effect in man. A later study showed that the psychoactive drugs in each group are capable of assuming conformations analogous to some part of the ring structures of LSD (Proc. US Nat. Acad. Sci., 60, 206; 1968).

Some experimental support for these theoretical studies has been provided by Smythies et al. (Nature, 226, 644; 1970), who found that THPC (which represents the D ring of LSD) will antagonize the behavioural effects of LSD, but greatly potentiates the effect of mescaline, which is a phenyl-ethylamine resembling the A and B ring portion of LSD. This suggests that mescaline occupies part of the site acted on by LSD, but that the complete structure is necessary for the full effect.

In the forthcoming issue of Nature New Biology (April 11), Smythies's team now report that behavioural effects of two amphetamine derivatives support the notion of a common site of action. Using an animal behaviour task (Sidman avoidance), they compared the psychomimetic activity of stereoisomers of 2,5 dimethoxy-4-bromoamphetamine (DOB) and 2,5 dimethoxy-4-methyl-amphetamine (DOM). Their reasoning was that if these two amphetamine derivatives, which show profound psychoactivity in man, act by way of a LSD-type receptor, then their R(−) isomers should have the greater effect because the R(−) conformation corresponds to that of LSD. The stereospecific approach is powerful because it controls for variations in the transport and metabolism of drugs. Presumably, only specific receptor sites would differ in their response to the subtle steric differences between the two isomers. In these experiments, the R(−) isomers of both DOM and DOB were considerably more active than the alternate S(+) configuration.

If subsequent investigations continue to support the notion of a common receptor for hallucinogenic drugs, then the central question will be: what is the endogenous neurochemical which is the true substrate for the "hallucinogenic receptor"?

fundamental knowledge of this kind may bring not only the ability to assess potential harm to the foetus from drugs consumed by pregnant women, but also the opportunity to practise foetal therapeutics. Dr R. A. Chez (National Institute of Child Health and Development, Bethesda) looked forward to further procedures such as those now being developed to treat, for example, foetal erythroblastosis and respiratory distress in newborn infants through medication of the mother before birth.

WRASSES
Cleaning Symbioses
from our Marine Vertebrate Correspondent

THE discovery that some fishes enter into symbiotic relationships with others whereby they clean their hosts of parasitic and fungal infections was essentially a by-product of the development of compact underwater breathing apparatus. The freedom this gave to biologists to observe fish behaviour untrammelled by captivity quickly led to several observations of fishes, especially wrasses (family Labridae), which specialize in this symbiotic relationship. Many cases have been reported in tropical seas but recent studies show it to occur in temperate seas, as off New Zealand (see *Nature*, **238**, 433 ; 1972) and in European freshwater fishes (E. F. Abel, *Oecologia* (Berl.), **6**, 133 ; 1971). More recently G. W. Potts (*J. Mar. Biol. Ass. UK*, **53**, 1 ; 1973) has found that several north European marine fishes may be involved in cleaning symbioses.

Potts reports observing the shallow water wrasse *Centrolabrus exoletus* pecking at the sides of a ballan wrasse *Labrus bergylta* posturing in the fashion adopted by host fishes soliciting the attention of a cleaner. Three wrasses were inspected and cleaned by this *Centrolabrus* specimen, operating in a shallow sublittoral region on the Devon coast. Potts also reports cleaning behaviour by several species of wrasse, and other species, in the tanks of the public aquarium at the Plymouth Laboratory. The species involved were the goldsinny, *Ctenolabrus rupestris*, and the corkwing wrasse, *Crenilabrus melops*. Free-living specimens of the latter from the Plymouth region have been found to contain in their stomachs the externally parasitic praniza larvae of certain crustaceans, which suggests that cleaning symbiosis is part of the way of life of this species. In the aquarium *Crenilabrus melops* became active soon after the aquarium lights were switched on each morning and approached various fishes which responded by invitation postures. Many of the host fish carried the praniza larvae of the crustacean *Gnathia maxillaris*, adults of which live in the gravel of the
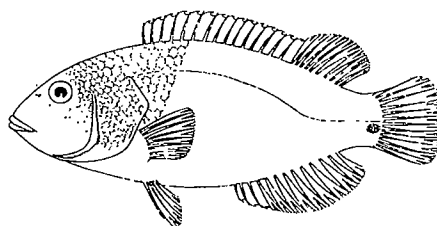
Corkwing wrasse, *Crenilabrus melops*.

aquaria. The wrasse were evidently removing these nocturnally-active parasitic larvae from their hosts.

It is doubtful, however, to what extent Potts's observations are referable to natural conditions. The fish associations of this aquarium—mackerel, black sea bream, red sea bream, plaice, ballan wrasse and corkwing wrasse are mentioned — are unlikely to be found in nature. The evident abundance of the praniza larvae of *Gnathia maxillaris* is also possibly an artefact of aquarium life. If anything, these observations suggest that even in temperate waters some wrasse species have a tendency to enter into a symbiotic cleaning relationship with other fishes. In free-living conditions this tendency may well remain mostly latent, but in the aquarium the adaptable, and opportunist, feeders such as *Crenilabrus* and *Centrolabrus* may take advantage of the opportunity to clean other fishes.

It is noticeable that most of the cleaners described among tropical (and the New Zealand) wrasses have contrasting dark markings, a condition which has led to the suggestion that cleaner fishes have distinctive "guild mark" coloration. Both the temperate European species which Potts has shown can act as cleaners have distinctive dark markings on the sides of the body. Other wrasses in British waters have similar dark contrasting markings either during their juvenile stage or throughout life. It would be worthwhile investigating whether they too act as cleaners, for whether they too act as cleaners.

TUMOUR VIRUSES
Origin of New Isolate
from our Cell Biology Correspondent

RD114 virus is a C-type RNA virus which contains 60–70S single stranded RNA and reverse transcriptase. It is liberated from RD114 cells which have a human karyotype and which were derived from a tumour induced in a kitten by inoculations of RD cells. RD cells were in turn derived from a human rhabdomyosarcoma ; they have been adapted to continuous growth in culture and they do not liberate detectable C-type particles. This is, of course, a familiar story to anybody who has followed the search for human RNA tumour viruses, and the question of whether or not RD114 virus is of human origin or a feline virus or even some

recombinant human/feline virus is still open. What is known is that the antigens and reverse transcriptase of RD114 virus are not related either to the antigens and enzyme of feline leukaemia and sarcoma viruses nor to the antigens and enzyme of primate (woolly monkey and gibbon) C-type RNA viruses.

In an attempt to throw light on the question of the origin of RD114 virus Todara *et al.* (*Proc. US Nat. Acad. Sci.*, **70**, 859 ; 1973) obtained RD cells from McAllister who, with his colleagues, isolated them as well as RD114 cells and RD114 virus and transplanted them into NIH Swiss mice that had been immunosuppressed with antithymocyte serum (AT). The immunosuppression, of course, allowed the human RD cells to grow in a heterologous species. The tumours that developed in immunosuppressed NIH Swiss mice inoculated with RD cells could be explanted and grown in culture or passaged in further mice.

Todaro found that a cell line established from a third generation transplant tumour liberated a C-type virus. RD cells as noted earlier do not liberate C-type viruses, and NIH Swiss mice have a low incidence of leukaemia and have never been reported to produce C-type viruses even though some viral information is expressed. What then is the origin of this virus, called AT124, which is liberated by RD cells after passage in NIH Swiss mice and how if at all, is it related to RD114 virus?

AT124 virus proved to have a host range comparable with that of RD114 virus. Both viruses grow well in cat, primate and human cells but fail to grow in murine cells including NIH/3T3 cells. AT124 virus, however, contains murine virus reverse transcriptase, or to be more precise reverse transcriptase sensitive to inhibition by antiserum raised against murine reverse transcriptase, whereas the reverse transcriptase of RD114 virus is not related by any known criteria to feline virus reverse transcriptase. AT124 virus particles also contain the group specific antigenicity unique to murine C-type RNA viruses, whereas RD114 virus particles do not contain the corresponding feline antigenicity. Finally AT124 virus can act as helper for the replication of murine sarcoma virus.

These data clearly indicate that AT124 virus is quite closely related to the murine leukaemia viruses ; indeed it is possible that AT124 virus will prove to be an endogenous virus of NIH Swiss mice. A second explanation of the origin of AT124 virus is, however, more attractive. Todaro and his colleagues found that ten other sorts of human tumour cells could be transplanted into NIH Swiss mice but none of the tumours that arose in the mice liberated C-type virus. Neither do chronically immunosuppressed NIH Swiss mice liberate C-type particles. These observations in-

dicate that the human RD cells contribute some function which allows the complete replication of C-type viruses. One can speculate for example, that cells of NIH Swiss mice contain an endogenous but replication-defective viral genome that by recombination with some part of the RD cell genome acquires the ability to replicate in RD cells.

Obviously there are other ways of explaining the origin of AT124 virus, but it should be possible to decide between the various alternatives by comparing the nucleic acids and antigens of RD114 virus, AT124 virus, primate, feline and murine leukaemia viruses and the endogenous C-type viruses that can be induced from primate, feline and murine cells by chemical and physical mutagens and carcinogens. Currently the betting seems to be that both RD 114 virus and AT124 virus will prove to be recombinant viruses derived from human and, respectively, feline and murine C-type virus genetic information.

AMPHIBIA

Centenarian Triton

from our Soviet Correspondent

THE alleged discovery in the Kolyma region of a Siberian triton, a form of newt, which had apparently hibernated in a block of ice, and came to life when the ice was melted was at first treated with considerable scepticism by Soviet biologists. These doubts, according to a report in *Izvestiya* (No. 66, 1973) have now been allayed, and a long hibernation of the order of a century—some ten to fifteen times the triton's normal lifespan—is now accepted.

The discovery, at the depth of 11 m, of the triton in its ice was reported to geologist D. Kolomiytsev, who was working in the area, and who communicated the news to N. Shcherbak, head of the Zoological Museum of the Ukrainian Academy of Sciences. Shcherbak agreed to study the triton, which was dispatched to Kiev, still alive, in an improvised container consisting of a moss-lined briefcase.

Superficial inspection showed the triton to be of a brownish colour, with a bare glistening skin, and to have a considerable aversion to light. Detailed radiocarbon studies, made by Shcherbak and his colleague N. Kovalyuk from the Ukrainian Institute of Geochemistry and Mineral Physics, gave the triton's absolute age, calibrated against readings for several other animals of known ages, of close to a century.

Asked to comment on the significance of the discovery, Shcherbak was non-committal. He stressed, however, that it raises extremely interesting questions related to the conservation of living tissues and of the whole organism.

MESSENGER RNA

Thirteenth Stroke

from our Molecular Biology Correspondent

JUST as it is only the thirteenth stroke of the clock that casts doubt on the validity of all that has gone before, the body of evidence amassed in recent years on the affinity between mitochondria and bacteria receives a bad shaking from new revelations of Perlman, Abelson and Penman (*Proc. US Nat. Acad. Sci.*, **70**, 350; 1973). The identification of mitochondria with primaeval symbiotic bacteria is based primarily on features of the mechanism of protein synthesis. The arguments, it must be owned, are strong: in particular the ribosomes are small (at 60S actually smaller than those of bacteria), initiation of protein synthesis is thought to require a formylmethionine tRNA as in bacteria (or at least formylmethionine has been found in the mitochondrion), and response to the inhibitors, cycloheximide and chloramphenicol, is of the kind expected of bacterial rather than eukaryotic systems. Perlman *et al.* have now isolated the messenger RNA from mitochondria of HeLa cells and were evidently taken aback to find that it contains a tract of polyadenylic acid, a feature absent from bacterial messengers, but characteristic of those of animal cells.

The key to the success of this work was the use of the drug camptothecin, which arrests the synthesis of high-molecular weight nuclear RNA, but does not disturb the activity of the mitochondria. Radioactive label then enters only the mitochondrial RNA, as confirmed by the disappearance of label under the action of ethidium bromide, which is again specific for mitochondrial RNA synthesis under the right conditions. Moreover this labelled RNA adheres to the membrane fraction, and is not susceptible to degradation by pancreatic ribonuclease until the mitochondrial membrane is disrupted. The radioactive profile, after gel electrophoresis of the RNA, shows two peaks corresponding to the larger and smaller ribosomal components, and a polydisperse spread of other species. Chains with a sufficiently long tract of polyadenylic acid can be caught on filters containing immobilized polyuridylic acid, and retention of mitochondrial RNA on such matrices was demonstrated. Isolation of the poly (A) segment by treatment of the RNA with pancreatic and T_1 ribonucleases, followed by gel electrophoresis, shows that the molecular weight is rather low, being estimated to correspond to some 50–80 residues, compared with perhaps 200 in cytoplasmic messengers. That the poly (A) is indeed associated with mitochondrial messenger is shown by its sedimentation with the polysome fraction, from which it is liberated by addition of puromycin.

Because the mitochondrial messenger never leaves the mitochondrion, the observations tend also to explode the hypothesis that the poly (A) acts as a carrier during the peregrination of the messenger from nucleus to cytoplasm. It is possible of course that the poly (A) segments may have more than one function, and Perlman *et al.* note that the mitochondrial messenger has the short length of its poly (A) in common with two viral RNAs: here again no transport process precedes utilization. A short poly (A) run has also now been found in a messenger RNA by

Replication of Poliovirus RNA

MANY, perhaps most, messenger RNAs that are translated in mammalian cells contain polyadenylate (poly (A)) tracts and in poliovirus particles the single stranded RNA, which serves both as messenger and as genome, is no exception. It has a 3'-terminal poly (A) tract and, according to experiments reported by Yogo and Wimmer in *Nature New Biology* next Wednesday (April 11), this poly (A) is probably transcribed from poly (U) sequences in the minus strand of the polio replicative intermediate which may be a circular structure.

Yogo and Wimmer showed that the plus strand RNA of the linear replicative intermediate has a 3'-terminal poly (A) tract longer than the poly (A) tract of RNA from virions. Furthermore, at the 3' end of the complementary minus strand there is a tract of poly (U). The linear replicative intermediate must therefore be a double stranded molecule with single strand 3' tails at opposite ends, the plus strand tail being poly (A) and the minus strand tail being poly (U). Clearly a 3'-poly (U) tract on the minus strand cannot act as template for a 3'-poly (A) tract on the plus strand. The minus strand poly (U) must be 5' terminal to act as template for the 3'-plus strand poly (A).

To resolve this dilemma Yogo and Wimmer speculate that the replicative intermediate molecule may be circular. They suggest that during replication of poliovirus RNA the infecting parental plus strand acts as template for the synthesis of a complementary minus strand with 5' poly (U). They further suggest that the minus strand is circularized by a putative RNA ligase before it acts as template for synthesis of progeny plus strands with 3'-terminal poly (A) and that breakage of this circular replicative form could yield linear minus strands with 3' rather than 5' poly (U) tracts.

McLaughlin et al. (J. Biol. Chem., **248**, 1466; 1973), and this is a case of particular interest, for it concerns the primitive eukaryote, yeast. The appearance of poly (A) in this cell suggests that it may be a common feature of all eukaryotes, and not only mammalian cells (though the absence of poly (A) from messenger specific for histones has been reported).

McLaughlin et al. followed the incorporation of label into the RNA, and have isolated the poly (A), after nuclease digestion of the rest of the chain, by adsorption on poly (T) coupled to cellulose. As a pretty demonstration that the poly (A) is a part of the messenger they have used a temperature-sensitive mutant, and shown that under nonpermissive conditions at 36° C the adenine label, previously incorporated at 23° C, is displaced from the polysomes and sediments with free ribosomes. Moreover after dissociation of poly (A)-containing polysomes, all the poly (A) is found with the polydisperse messenger fraction. Another facet of this work is the application of a superior method of molecular weight estimation. Rather than merely use a sedimentation or electrophoresis procedure, with the hope that a calibration based on the usual RNAs will apply, they have performed end-group determinations. Chromatography of the product of alkaline hydrolysis, and comparison of the counts in adenylic acid and adenosine, showed in the first place that the poly (A) run was at the 3' end of the RNA as in other eukaryotic messengers, and that the chain length was of the order of fifty nucleotides. An interesting additional observation is the failure of the entire messenger fraction to bind to the poly (T), and the absence of poly (A) from the part that does not bind. The integrity of the ribosomal RNA components indicates that this is not the result of nuclease activity, and it may present a parallel to the case of histone messenger. The variety of possible roles for the poly (A) tract of the messenger is now a subject of speculation, and no doubt new experimentation.

A variant of the end-group method has been used to identify poly (A) at the 3' end of the HeLa cell messenger and of heterogeneous nuclear RNA, by Nakazato, Kopp and Edmonds (ibid., 1472). Here the terminal sugar is oxidized with periodate, and the resulting glycol reduced with tritiated borohydride, so as to introduce an end-group label. The bulk of this label is recovered in the nuclease-resistant poly (A) fraction. In addition, however, the heterogeneous nuclear RNA appears to contain a short run of poly (A), some twenty residues long, which is not by the same criteria at the 3' end. The presence of the bulk of the poly (A) at

this end of the nuclear RNA supports the view that the messenger comprises the 3' end of the precursor.

CONSERVATION
Sheep or Grouse ?

from our Plant Ecology Correspondent
CONSERVATION involves the practical management or manipulation of ecosystems in such a way that a predetermined ecological goal can be achieved. The goal itself is often selected on aesthetic, emotive, or economic grounds rather than scientific ones. A good example of this principle at work is found in the current issue of Biological Conservation (**5**, 41 ; 1973), in which Watson and O'Hare describe experiments designed to "improve" the Irish blanket bogs.

The experiments which they describe are aimed at increasing the red grouse population of the Donegal and Mayo bogs with a view to improving the shooting potential of the area and hence enhancing tourism. The experiments consist of fencing plots to exclude grazing animals and fertilizing them with superphosphates (502 kg ha^{-1}), potassium sulphate (125 kg ha^{-1}) and smaller quantities of other nutrients. Some plots were also drained. Two years after draining and fertilizing, heather (the staple food of the red grouse) had a productivity four times that in control plots and the phosphorus content of its tissue was twice that of the controls. The density of grouse in the treated areas had also increased by a factor of two and their breeding success was three times that of birds in control areas.

As a management system for increasing the density of grouse in the short term, drainage and fertilization must be considered a most effective treatment. The authors do not, however, stress the fact that these results were obtained in the absence of stock grazing. This is unfortunate, for the work of Watson in Scotland (Nature Conservancy Research in Scotland, Report for 1968–70, NERC) demonstrates that without the exclusion of grazing animals, fertilization produces no change in the population density of grouse. The choice, therefore, seems to be sheep or grouse.

There are other ecological questions which should be raised with respect to this work. Watson and O'Hare have found that heather under low phosphate conditions responds well to added phosphate. In natural ecosystems, however, a species which can survive, even at suboptimal growth, in a poor environment may be at a considerable advantage in avoiding competition from more aggressive species. Raising the nutrient status of a bog ecosystem could destroy this balance and lead to the displacement of heather by more nutrient-demanding, vigorous plants. The long-term effects of drainage and fertilization could be harmful, even to grouse. Eutrophication of many systems has a short-term beneficial influence on productivity which is not maintained.

In western Ireland the economic consideration must be paramount in selecting an appropriate management system. The authors are unwise, however, in suggesting that such a system would also result in improved conditions for wildlife in general. This type of management is likely to benefit only the grouse and the shooting fraternity.

New Case of Disulphide Degeneracy

THE proteolytic enzyme, papain, as conventionally prepared, contains the active enzyme, with a free thiol group at position 25 in the chain, an inactive component, which can be activated by exposure to reducing agents, and a dead fraction in which the vital thiol is thought to be oxidized. By eliminating protective thiols from the preparation, Brocklehurst and Kierstan have isolated a fraction which contains some thiol groups, but is nevertheless inactive: they report their findings in next Wednesday's Nature New Biology (April 11).

Whereas the thiol group in active papain is highly reactive towards a disulphide reagent, dipyridyldisulphide, even at acid pH, that of the inactive fraction behaves differently, the pH-reaction rate profile corresponding to pK of 7.6. When reduced this material is converted to normal active papain.

Reaction of the thiol groups with radioactive isodoacetamide, followed by reduction, showed that two different types of thiol groups, in respect of pH-reactivity dependence, are present in the activated species. This can be interpreted to indicate that in the thiol-containing inactive species, cys-25 is involved in a disulphide bond with one of the other six half-cystines in the molecule, and that conversion to the active enzyme ensues by thiol-disulphide exchange.

A detailed activation scheme involving thiol-disulphide exchange between the active site cys-25 and residues at positions 22 and 63 is suggested. Two other proteins with the rare property of containing both cystine and cystine residues, have previously been shown to exist in structurally degenerate states, in which alternative disulphide pairings occur.

MAMMAL-LIKE REPTILES

Lines of Evolution

from our Vertebrate
Palaeontology Correspondent

THE lineage of the mammals, through the mammal-like reptiles or synapsids, has been distinct from that of other reptiles for as long as reptiles are known to have existed—since the Lower Pennsylvanian, more than 300 million years ago. Reisz (*Bull. Mus. Comp. Zool. Harv.*, **144**, 27 ; 1972) has recently supported the view that *Protoclepsydrops*, from the Lower Pennsylvanian of Nova Scotia, is probably a synapsid. He also describes a variety of synapsids from the Middle Pennsylvanian of the same area, which show that the radiation of the group had already begun by that time. One of them, *Archaeothyris*, is very similar to the Lower Pennsylvanian primitive reptile *Hylonomus*, differing chiefly in possessing the synapsid temporal opening. Reisz notes that this opening permits a more efficient use of the jaw musculature, allowing the jaws to be opened more widely and closed more rapidly. He suggests that this was an important factor in allowing the increased size that characterized the Permian synapsids, and enabled the group to become the dominant reptiles of that age.

Study of the remaining mammal-like reptiles has long been hindered by two factors. The first is the lack of adequate links between the Lower Permian forms and their Upper Permian descendants. This void was to some extent filled by the discovery of a Russian fauna, intermediate in both structure and age. Proper understanding of their relationships with the Upper Permian synapsids, however, has still been slow to appear, because of the second difficulty. Ironically, this has been the superabundance of material in the Upper Permian Karroo fauna of South Africa. Presented with an exhaustible supply of new material, chiefly skulls, such earlier workers as Broom produced a stream of reports in which the external cranial features were used as the basis for the erection of new taxa, often using characters which today seem trivial and unreliable. To describe the internal anatomy of the skull, or the postcranial skeleton, would have necessitated more time-consuming mechanical methods for preparing the material.

Only recently have palaeontologists at last begun to reduce the vastly inflated list of South African genera and species of mammal-like reptiles, and more refined methods of preparation are also making it possible to study in more detail such aspects as cranial mechanics. To take as an example the gorgonopsians—carnivorous forms with large stabbing teeth — Sigogneau (*Cahier Pal.*; CNRS, Paris, 417 pp ; 1970) has reduced the original sixty-seven genera to a mere twenty-six valid genera, plus eleven genera of uncertain position (most of which are not even determinable as gorgonopsian!). The functional anatomy of the Gorgonopsia, especially their jaw mechanics, has been studied by Kemp (*Phil. Trans. Roy. Soc.*, **B256**, 1 ; 1969). He concludes that the group is so distinct from the other advanced synapsids (the therocephalians and the cynodonts) that it should be raised to the rank of a suborder, the other two groups remaining in the suborder Theriodonta. Sigogneau's work accepts earlier views that a few of the gorgonopsians belong in a separate group, the ictidorhinids. In a joint article, Sigogneau and Tchudinov (*Palaeovertebrata*, **5**, 79 ; 1972) suggest that these two types of gorgonopsians may have evolved from two separate groups of the known Russian earlier mammal-like reptiles.

In a more recent report, Kemp (*Phil. Trans. Roy. Soc.*, **B264**, 1 ; 1972) supports the view of some earlier workers that the cynodonts evolved from the therocephalians. He believes, however, that the therocephalian ancestor was an early whaitsiid—a rather late group which is usually regarded as highly specialized. Kemp's theory is not without its difficulties, but it does provide a new approach to the problem of cynodont ancestry.

The cynodonts themselves are of particular interest, because it is from this group of mammal-like reptiles that the mammals evolved. Their classification has recently been revised by Hopson and Kitching (*Palaeont. Afric.*, **14**, 71 ;

Variations in Variscan Granites

IN two recent articles, Hall (*Contr. Mineral. Petrol.*, **32**, 186 ; 1971 and *Mineral. Mag.*, **38**, 847 ; 1972) has suggested that the differences in the average compositions of the granites in the Variscan, Caledonian and Alpine orogenic belts, and the compositional variations within the Caledonian belt, may both be attributed to variations in the geothermal gradient. In *Nature Physical Science* this week (April 2), he takes these studies a stage further by showing that the correlation within the belt between composition and geothermal gradient also applies to the Variscan granites.

The compositional part of the correlation is represented by trend surfaces (up to the sixth degree) for normative quartz and albite, based on chemical analyses of all those granites with reasonably certain Variscan ages and taking account of the post-Variscan rotations of Iberia, Corsica and Sardinia. In the case of normative quartz, the trend surfaces for all six degrees are highly significant statistically (>95 per cent confidence level) and so the sixth degree surface, which exhibits regional variations down to the 100 km scale, was chosen for the actual correlation. For normative albite, confidence levels fall off rapidly from the fourth degree onwards and so the third degree surface (>99 per cent) was used for correlation purposes.

The corresponding Variscan geothermal gradients have been assessed on the basis of the relative degree of metamorphism, low and high pressure metamorphism being representative of high and low geothermal gradients, respectively. Low pressure metamorphism of Variscan age is present in most of the granites shown on the map, although convincing evidence of Variscan high pressure metamorphism is found only in the Hesperic Massif. The granites of the Hesperic Massif are, however, also the poorest in normative quartz and the richest in normative albite—in other words, these extremes correlate with the evidence for low geothermal gradients. The sense of this correlation is the same as that for the Caledonian orogenic belt.

Finally, Hall goes on to show that the Hesperic Massif in albite (rich and poor in quartz) is also the area where the granite magma developed under the highest water pressures. This fact ties in with his interpretation of the correlation between composition and geothermal gradient, which is that the various magmas formed by melting in the crust at a depth governed by the geothermal gradient. For a normal temperature gradient of about 30° C per km, the required temperature for a granitic melt at the base of the crust would only be reached if the melt were saturated with water. But for a higher geothermal gradient, either undersaturated melting would be possible at the base of the crust or melting at a lower degree of undersaturation would be possible higher up in the crust. Thus in general the relatively high geothermal gradient corresponds to a magma with a relatively low water pressure, and vice-versa.
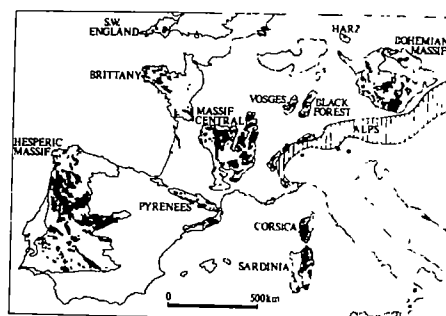
The distribution of granites (black areas) in the Variscan massifs (shown in outline) of western Europe.

1972), who include both the herbivorous tritylodonts and the carnivorous tritheledonts ("ictidosaurs") as end members of the group. Within the cynodonts, mammalian ancestry seems to have lain within the Brazilian family Chiniquodontidae, and Romer (*Breviora*, **344**, 1 ; 1970) has described the skull of a genus, *Probainognathus*, which may lie on the direct line of mammalian evolution. The postcranial skeleton of cynodonts, and the evolution of that of mammals, has recently been thoroughly described by Jenkins (*Bull. Peabody Mus. Nat. Hist.*, **36**, 1 ; 1971).

Though much work remains to be done, particularly in elucidating the relationship between the therocephalian and cynodont stock and the Russian earlier forms, the principal lines of evolution of the mammal-like reptiles, and the adaptive reasons for their structural divergences, are now becoming steadily clearer.

PSYCHOLINGUISTICS

Learning Syntax

from our Experimental Psychology Correspondent

THE view of language acquisition that one derives from Chomsky's emphasis on syntax is that of a child acquiring a working theory of grammar, by being equipped initially with a set of hypotheses between which he has to choose on the basis of the rather small set of utterances he hears. In this sense, as Chomsky points out, the child's task is not logically different from that of the linguist constructing a theory of grammar. A quite different view would be that children do not discover the syntactic rules of a language by finding the underlying regularities of strings of sounds, but that they use their understanding of the semantic setting in which utterances are made to understand words and the significance of their grammatical relationships.

This second view seems a good deal more plausible, but there is the difficulty of describing exactly what kinds of semantic arrangement give rise to grammatical rules. It is in this context that two recent articles by Moeser and Bregman (*J. Verb. Learn. Verb. Behav.*, **11**, 759 ; 1972 ; and **12**, 91 ; 1973) are of interest. In their experiments Moeser and Bregman taught first college students, and then school-age children a miniature artificial language, which had a simple underlying grammar consisting of a small set of rewrite rules. The language was taught by exposing subjects successively to well formed sentences in that language, or by exposing them to this same set of sentences plus pictures of possible

referents for the language. The words in the language were nonsense syllables, and the syntactic rewrite rules were of the form $S \rightarrow AP + BP$; $AP \rightarrow (D) + A$ and so on: meaning that a sentence S can be rewritten as an A phrase followed by a B phrase ; an A phrase is a D followed by an A and so on. After exposure to each block of eighty well-formed examples, subjects were asked to make judgments of which of a pair of test sentences (without pictures) were grammatically correct, where neither of the test sentences had previously been seen.

In their first experiment Moeser and Bregman compared performance among four groups of subjects shown (1) words only, (2) words plus a row of arbitrary pictorial figures, with each one always corresponding uniquely to a word, (3) words plus a row of figures each displaying a property referred to by the word, and (4) composite figures using these same reference classes as (3), but made up in such a way that the logical constraints of the pictures were mirrored by the syntax rules. Thus a two-word A phrase YOW FET would have as the pictorial referent in its (3) condition a dotted line and, separately, a green rectangle, but in its (4) condition it would have these reference classes combined to form a green rectangle bounded by dotted lines. In their first experiment they found increasing ease of learning the syntactic rules across the conditions (1) to (4).

In their second experiment Moeser and Bregman gave much longer practice with a total of 3,200 presentations of well-formed sentences, and compared simply the equivalent of conditions (1) and (4) in six subjects who were somewhat younger (aged 12 to 18) than those of the first experiment. Here the results were much more clear cut. Whereas the three subjects trained only with words performed at or near chance with the pairs of test sentences, those trained with words and semantic referents approached completely correct judgments on the grammaticality of the test sentences. The subjects who had successfully learned the syntactic rules with the help of semantic referents were furthermore able to learn the syntactic categories of new words each presented in just three novel sentences without pictures. Subjects trained in the words-only condition did not learn the syntactic categories of the new words.

This sort of experiment does not, of course, show that syntax is learned by appreciating the semantic constraints of referents, but it does show that grammar can be learned much more easily when this is possible. It would be surprising if this were not made use of in a child's initial acquisition of language.

MARS

Up Hill Down Dale

from our Soviet Correspondent

PHOTOMETRIC data from the Mars 2 and Mars 3 probes have provided new estimates of the heights of surface features on the planet. The method is based on the measurement of reflected solar radiation in the CO_2 bands at 2.06 μm and 2.01 μm, and in the continuous spectrum around 2.25 μm. The pressure of CO_2 on the surface is determined from the intensity of the bands, and hence the height of the surface at that point may be calculated from a barometric formula.

The method has already been used in observations from Earth, but a resolution of only 500 to 1,000 km was obtained. Results of this kind for individual areas of the Martian surface, with considerably better resolution, were obtained by Mariners 6 and 7. The Mars 2 and 3 experiments were intended to give a continuous scan of the planet's surface using a field of vision of 0.01 rad (15 km from a distance of 1,500 km), although some averaging of results was carried out before data transmission so that each averaged reading corresponded to some 50 km of flight of the spacecraft.

Reporting their data (*Doklady Akad. Nauk SSSR*, **208**, 1048 ; 1973), the team from the Institute of Space Research of the Soviet Academy of Sciences stress that the results are "preliminary".

Working with the 6 mbar isobar as an arbitrary baseline, they quote data for the Mars 3 trajectory of February 16, 1972, which passed over the northern extremity of Hellespontus, the north-west edge of Hellas, the dark regions Iapigia and Syrtis Major, and also Meroe and Umbra and the north polar cap. They report a maximum height for Syrtis Major (+3.5 km) and minimum heights for Hellas (−1 km) and the region to the north of Syrtis Major (0 to +1 km). North of 50° N the presence of the polar cap introduces considerable anomalies in the equivalent band width of CO_2. Comparison of these data with those of the similar trajectory of December 27, 1971, shows that on the earlier date, during the dust storm, a considerable decrease in the band width was observed, confirming earlier observations from Earth made by one of the present team (Moroz) and by Parkinson and Hunten (*Science,* **175**, 323; 1972).

The Mars 3 trajectory of February 28, 1972, passed over Nereidum Fretum, Mare Erythraeum, Margaritifer Sinus, Chryse and Mare Acidalium, and also gave an anomalous reading for the north polar cap. In the equatorial zone, altitudes were considerably less than those recorded on February 16, 1972,

which confirms radar and spectroscopy measurements from Earth. The greatest difference between the readings for the two tracks was approximately 6 km. The Soviet data for the region of latitude 40° S differed considerably from the Mariner 6 ultraviolet readings, which gave heights some 3 km lower. This may have been the result of a local ultraviolet haze during the Mariner 6 readings.

LAKES AND SEAS
Surface Circulation

from a Correspondent

IN a recent issue of the *Proceedings of the National Academy of Sciences* (**70**, 93 ; 1973) Emery and Csanady report their investigations of the surface circulation of forty lakes, marginal seas, estuaries and lagoons, all in the Northern Hemisphere. Their studies are based on records obtained by various means, such as surface drifters, current meters used from anchored ships, drogues, buoyed fishing nets, and theoretical calculations based on the temperature and salinity stratification. Few, if any, of these results were based on their own measurements. They find that with one exception, that of the Aral Sea (45° 00' N, 60° 30' E) in the Soviet Union, the circulation is always anticlockwise if the mean is taken over a sufficiently long time. The examples include all the Great Lakes, Lake Constance, Lake Geneva, the Caspian Sea and the Dead Sea, and the marginal seas include the Baltic Sea, the Black Sea, the Adriatic Sea, Hudson Bay and the Persian Gulf. Unfortunately no records were obtainable for the Southern Hemisphere, but the implication is that the circulation there is clockwise.

Emery and Csanady discuss various mechanisms by which such a circulation could be set up. They discount the effect of long surface waves and internal waves, even though these would be propagated in an anticlockwise direction, for their effects would average out over the times considered. They ascribe the effect instead to Ekman drift. This follows from Ekman's theory of wind-driven currents, which was propounded in the early 1900s and allows for the effect of the Coriolis force. This arises because in establishing and using equations of motion based on a set of axes fixed on Earth rather than in space there seems to be a force acting towards the right of the direction of movement and proportional to the speed when there is motion with respect to these axes. Ekman showed that when the wind acts on water for a long time, this force has to be counterbalanced by a movement of water to the right of the wind direction. This movement is called the Ekman drift. It is then suggested

that when a temperature-stratified water basin is heated while under the action of the wind, there is, looking along the wind direction, a movement of warm surface water from left to right and the water on the left is replenished by colder water ascending from underneath. In the end the right side of the basin has warmer surface water than the left.

Emery and Csanady then go on to suggest, further, that the drag of the wind on the water surface depends strongly on the difference between the temperature of the air and of the surface water. When the air temperature is less than that of the water, the air close to the water surface tends to become warmer than the air above and ascends. This leads to the formation of eddies and turbulence which increase the frictional effect of the wind. Thus under certain conditions the wind drag on the right of the water basin would be greater than on the left and so there would be a net anticlockwise circulation.

This theory is quite a plausible one. It is, however, possible to argue against the view that the effect of internal waves can be neglected ; I have recorded such waves with a period of 48 h in a relatively small lake and there may well be some with even longer periods in the basins considered by Emery and Csanady. The amplitude of these waves would depend on the stratification and this could change significantly during the wave period and so lead to asymmetry and a net current transport. The validity of this view depends on the length of time for which the records have been taken, and this is not stated. The anomalous behaviour of the Aral Sea may be a consequence of some such effect.

SEDIMENTOLOGY
Tectonic Control

from our Structural Geology Correspondent

IT is seldom that cross-fertilization between different scientific disciplines is as successful as that demonstrated by Friend and Moody-Stuart (*Skr. Norsk Polarinst.*, **157** ; 1972) in their intricate analysis of Devonian palaeogeography in Spitsbergen. They chose for their analysis the Wood Bay Formation, the most extensive formation in the 8 km thick late orogenic Silurian and Devonian red bed succession in Spitsbergen. The formation is 3 km thick, outcrops over an area 150 km by 75 km, and represents deposition in river channels and clay flats (playa lakes). They collected field data relating to river palaeocurrents, the sandstone composition and the variation in grain size and plotted contours for these variables by means of a computer-based iterative-fit quadratic trend surface analysis. The results of this initial analysis showed that, in the east, rivers flowed into the alluvial area from the south-east carrying a high proportion of bed-load cross-stratified sands characteristically containing orthoclase feldspar, whereas in the west the rivers flowed from the west depositing a significant proportion of suspended-load sediment characterized by flat-laminated siltstones.

Having reached this stage in the analysis of the alluvial areas Friend and Moody-Stuart attempted to extend the palaeogeography by reconstructing the situation in the source areas. They used laboratory studies of water flow and knowledge of present rivers to interpret the characteristics of the Wood Bay

Structure of 1,1-Cyclopentanedicarboxylic Acid

IN an article in next Monday's *Nature Physical Science* (April 9) Margulis *et al.* report how many physicochemical techniques—X-ray diffraction and several kinds of magnetic resonance—have been brought to bear on a study of the problem of molecular motion in the solid state. They have examined crystals of 1,1-cyclopentanedicarboxylic

acid $(C_5H_8(COOH)_2)$ and also the cyclopentyl-1-carboxylic acid radical and have come to the conclusion that at room temperature the radical undergoes "pseudorotation". The five-membered ring of the molecule also turns out to be disordered, probably as a consequence of pseudorotation.

The basic ring of cyclopentane, C_5H_{10}, has been known for many years to consist of two puckered formations which have about the same energy, about 5 kcalorie mol^{-1} smaller than that of the planar formation. And it is also a well established idea that the puckering can be thought of in terms of a rotation of the phase of the puckering around the ring, "pseudorotation".

The electron density map produced by Margulis *et al.* of 1,1-cyclopentanedicarboxylic acid, viewed along the molecular and crystallographic two-fold axis, is shown in the diagram.
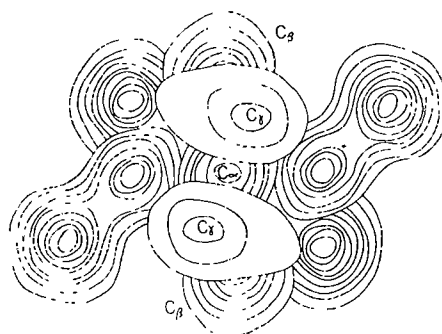
rivers in terms of the dependent variables of channel type, depth, flow strength and slope.

The profiles of rivers existing today are known to be strongly related to the nature of the sediment load that the rivers carry. Rivers carrying a bed load have braided, almost straight, channels and are some sixty times as wide as they are deep, whereas rivers carrying a suspended load or a mixed load have channels which meander and have a smaller ratio of width to depth (about ten). The depth of a river channel is given by the thickness of an individual graded sand cycle which is deposited by the river in a single unit during flood conditions. Thus Friend and Moody-Stuart were able to recognize two distinct river systems. An eastern one was characterized by bed-load braided channels, averaging, at the high stage, at least 2 to 3 m in depth, 120 to 170 m in width, and low sinuosity. The regional slope was gentle (15 cm km^{-1}) and towards the north-north-west. The western system was a complete contrast, having channels with flood depths of about 0.7 m of mixed or suspended-load type. They were highly sinuous, and about 7 m wide, depositing sediment on a relatively steep slope (100 cm km^{-1}), which faced east-north-east, and extending from a source only a short distance away.

From these values pertinent to the two river systems the authors calculated the mean annual discharge from each and hence the relative size of the source areas; the eastern source area turned out to be about 400 times greater than the western one. From this information they plotted the source areas and obtained approximate limits on the relief from a knowledge of the total volume of the Wood Bay Formation derived by denudation from these source areas. Thus the eastern area occupied an area of some 10,000 km^2 extending some 200 km south-east of the present alluvial area and with a relief of ~6,000 m, whereas the much smaller western source area was ~25 km^2 with a relief of ~150 m.

The full significance of this reconstruction is not apparent until one realizes that the obvious source area for the Wood Bay Formation is the denuded Caledonian mountain system of Ny Friesland, situated immediately to the east of the Wood Bay Formation outcrop and separated from it by the north–south Balliolbreen Fault. These mountains have had at least 10 km of Heckla Hoek sediments and metasediments eroded from them, and orthoclase and heavy mineral detritus within the Wood Bay Formation is similar to that in the Heckla Hoek. Friend and Moody-Stuart suggest that sinistral late Devonian (Svalbardian) movement along the Balliolbreen Fault carried

Ny Friesland from a source position 200 km south–south-east of the Wood Bay Formation to its present position. This is in accord with earlier suggestions by Harland (*Phil. Trans. Roy. Soc. Lond.*, **258**; 1965) that late Devonian sinistral transcurrent movement affected the whole North Atlantic area.

PHYSICAL METALLURGY

EM *in extremis*

from our Materials Science Correspondent

IN 1938 two crystallographers, Guinier in Paris and Preston in London, independently found smudges on their X-ray Laue photographs prepared from age-hardened duralumin crystals, and independently postulated that the smudges were caused by thin plates, or "zones", of copper trying to precipitate out of solution in aluminium. (*Nature*, as so often, was in at the birth (**142**, 569, 570; 1938).) Thereupon Preston moved on to other interests (see his obituary in *Nature* recently (**238**, 362; 1972)) and it was left to Guinier to spend many years of painstaking X-ray diffraction piecing together the structural details of the formations which have ever since been known as Guinier–Preston zones—GP zones for short. X-ray diffraction, however beautifully used, is a somewhat inadequate instrument when one has to analyse a population of zones which differ in all their dimensions and even in their fine structure, and so the advent of thin-film electron microscopy in the 1950s brought about a revival of interest in GP zones: the hope was to observe them directly.

The difficulty was that the zones in their early stages were known to be ultra-thin, possibly only one atomic diameter thick, and this was quite beyond the resolving power of the

microscopes of 10 to 15 years ago. The zones are, however, surrounded by a field of elastic strain: this field is both the source of the hardening associated with the presence of the zones and the means by which it is possible to see the zones in an electron microscope. The strained aluminium lattice diffracts electrons either more or less efficiently than the unstrained lattice, and thus the photographs image the strain fields rather than the zones themselves—the smile instead of the Cheshire cat. The trouble was that a picture of the smile failed to carry any information about the Cheshire cat's teeth.

Now at last it is possible to see the zones themselves and thus to measure their length and thickness accurately. Two recent papers (Phillips, *Acta Metallurgica*, **21**, 219; 1973; and Phillips and Tanner, *ibid.*, **21**, 441; 1973) reproduce electron micrographs of GP zones at unprecedented resolution. The first report is concerned with Al-Cu, the second with a closely related alloy, Cu-Be. In each instance, (002) lattice planes of the matrix are imaged as sharp fringes at a spacing of about 2 Å; at an early stage of ageing, GP zones of monatomic thickness are revealed as disturbances of these fringes. In Cu-Be, the zones are shown up by local brightness reversal of the lattice fringes, whereas in Al-Cu, Phillips actually succeeded in demonstrating a localized reduction in lattice spacing near the zones, the direct expression of the associated strain field. This is a remarkable technical achievement in electron microscopy, and opens the way to a more exact interpretation of the early stages of age hardening; a start has already been made by using the observations to identify the zone dimensions corresponding to the maximum in electrical resistivity during the ageing of a Cu-Be alloy.

Radio Emission from Nebulae Around Stars

IN next Monday's *Nature Physical Science* (April 9) Hjellming, Blankenship and Balick report the detection of radio emission associated with the stars MWC 349 and RY Scuti. This confirms earlier observations of the sources at several radiofrequencies, and provides evidence that the radio emission comes from resolvable radio "nebulosities" with thermal radio spectra.

The observations now reported were made at 2,695 and 8,085 MHz with the NRAO interferometer. Neither source showed any signs of variability at these frequencies during the period of observation (October 1972 to February 1973 for MWC 349; February 19 to 28, 1973 for RY Scuti), both have the same kind of visibility function, and both were nearly unresolved at 2,695 MHz with the longest interferometer spacing

(2,700 m); this suggests sizes ≲ 3 arc s. There is also an indication of complex structure in both sources.

So it seems that the radio emission is definitely not coming from a point source in either case. The emission comes instead from compact regions surrounding each star, and Hjellming *et al.* point out that it would be incorrect to call these objects "radio stars" because they do not show the strong variability, indicating "an intimate relationship" with the underlying star, that the name has come to imply. These two sources have, in fact, some similarities to planetary nebulae with electron temperatures around 10^4 K, dominant emission measures of ~10^8 pc cm^{-6}, and in general similar properties to such well-known planetary nebulae as NGC 7027.

CAREERS FOR SCIENTISTS

Science Graduates Must Widen their Horizons

THE articles which appear on the following pages are designed to give students who are graduating this summer some assistance in choosing a career. This is the time of year when, traditionally, undergraduates are feverishly trying to decide between the merits of one employer and another, but this year, as in the past few years, there are fewer employers on the horizon and those that are in the market want many fewer new graduate employees than they did in the halcyon days of the early and mid-1960s.

But is the situation now improving? There is some evidence that this year's crop of graduates will find it easier to find a job than their predecessors did last year but it is clear that the prospects are not better in all areas. The message to job seekers is that the traditional avenues of employment are still constricted but that there are reasonable prospects outside the areas where scientists have tended to look for work in the past.

The British graduate had little difficulty in selling his skills until the late 1960s but he now finds that a degree is no passport to employment. The most difficult year for the new graduate was 1970–71 when the British manufacturing industries took on only 6,500 new graduates compared with the almost 8,000 who accepted employment in these sectors in 1968–69 and 1969–70. Although the figures for 1971–72 are not yet available it seems unlikely that they will differ significantly from those obtained for 1970–71, but the cheering note is that the manufacturing industries this year are expected to recruit to a greater extent than they have done in the past two years. The numbers will, however, still be lower than for 1968–70.

Most arts graduates have, since time immemorial, progressed from university to employment in which they have not directly used the knowledge which they acquired as undergraduates. But the scientist after graduating has always expected to apply his knowledge in a more direct fashion. But now this traditional type of employment for the scientists is becoming increasingly less available and in the long term it is probable that this is not wholly a bad thing both for the graduate and his employer. Whatever employment the graduate scientist enters into, and in recent years this has included banking, sales and accountancy which have always been the preserves of the arts graduates, he does not stop making use of his science. He is therefore most certainly not a lapsed scientist, for whatever such a person is he is not someone with a degree in science who is earning his living without directly applying the results of his training.

University careers officers have realized during the past two years that the job patterns for science graduates are changing and the slightly better prospects which this year's graduates face are a direct consequence in no small measure of the efforts which have been made by the universities to find alternative employment for the science graduates outside these traditional areas. Employers, who in the past saw no need for science graduates but who have recently taken scientists on to their staffs, should now be more open to suggestions that they should employ more scientists—presumably in jobs which were until a few years ago the prerogative of arts graduates.

In recent years the numbers of science graduates entering employment have decreased and, not surprisingly, there has been an increase in the numbers taking courses in teacher training after graduating to compensate for this. But the numbers continuing in academic study have remained substantially constant since 1969. One of the most startling statistics to emerge from the articles on the following pages, however, is that between 1970 and 1971 the percentage of first degree mathematicians and statisticians who took up scientific work, which does not include teaching, decreased from almost 32 per cent to 17.7 per cent (see page 380). Physicists also suffered a similar decrease in demand from 29.1 per cent in 1970 to 19.5 per cent in 1971 but biologists and medical students have suffered no such large change, for in 1971 19 per cent of that year's first degree graduates took up scientific work compared with 22.3 per cent in 1969 and 18.9 per cent in 1970. The higher degree graduates fared slightly better but mathematicians and statisticians were still not needed to carry out scientific work to the same extent in 1971 as they were in 1970.

Even if job prospects for scientists in science-based industries are not getting substantially better, there are at least no large scale predictions being made now that the situation must first get worse before it improves. But the job situation in the science-based industries is expected to improve although there is no one in the know who is prepared to be bold enough to set a time on this. It is, however, universally agreed that the heady days for science graduates which occurred in the early and mid-1960s will not return. But, that said, there is universal optimism that the present slump is only temporary. Scientists in the United States have also suffered the same setbacks, but in 1972 the chemical industry in that country broke all records and the industry is starting to move upwards again. The British chemical industry is expected to follow suit soon although it will, quite properly, take time to readjust afterwards before it begins to think of increasing its intake of new graduates. The long term prospects for the scientist in industry are therefore not altogether bleak.

Education and Career of the Science Graduate

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> The changing role of the science graduate will present a particular challenge to the university teacher, who will also have to come to terms with the somewhat changed conditions under which he may in future do his own research.

I WRITE this article in Japan. This statement is not a bizarre irrelevancy, for Japan illustrates dramatically how rapidly human attitudes can change and human energies be redirected. On August 15, 1945, the people of Japan heard with awe the Emperor's words of acceptance of the terms of surrender imposed by the Allies. Not many Europeans will have noticed that Emperor Hirohito concluded his statement with an exhortation to the Japanese people to "Unite your total strength . . . so that you may . . . keep pace with the progress of the world". On the time scale of human history Japanese ethos and values changed overnight from the militaristic to the pacific, and now Japan has transformed herself from a semi-feudal to a democratic state in which in 1972 the Director General of Higher Education and Science in its Ministry of Education could justifiably maintain "that in higher education in Japan, equal opportunity of education is offered to all boys and girls without distinction of the social standing and occupational status of the families they come from".

In this state with twice the population of Britain there are four times as many students in degree level courses as in Britain, and rather more than twice as many new graduates in science, engineering and technology are launched on to the labour market each year. Moreover, there is no doubt in the minds of the Japanese that this rapid progress towards mass higher education should be maintained. The stark contrast between this optimistic attitude, doubtless partly attributable to the buoyant economy, and our present cautious approach, which is partly associated with the seemingly diminished employment prospects of our graduates in science and engineering, prompts the following home thoughts from abroad.

A Few Facts

Table 1 illustrates the growth of higher education in Britain during the past decade and a half. Within the rapidly growing university sector, virtually all the entrants to which have at least two A-levels and many have three A-levels, the number of science-based students has, despite the swing away from science, been maintained at a slightly higher level than that of non-science-based students, and the output of graduates has been in the same ratio. Disregarding Japanese university students who are studying subjects not normally found in the curriculum of British universities, for example home economics, teaching and nursing, only about one third of Japanese students have been studying science-based subjects. Moreover, in the 1960s Britain doubled its output of graduate scientists, excluding medicine and allied fields, from all forms of higher education to reach about 26,000 in 1970, whereas the corresponding figure for Japan is 76,000. In Britain, however, these graduates are almost equally divided between "pure" and "applied" science, whereas, even allowing for the fact that many courses of study which are in engineering faculties in Japan would be brigaded under pure science faculties in Britain, the Japanese pure science graduates form a far smaller fraction of the total.

From 1945 to 1969 all reasonably competent new graduates in science, engineering and technology in Britain found it easy to secure congenial and adequately remunerative employment, chiefly either in industry or in higher education. The proportions entering each of these spheres of employment did, of course, differ from subject to subject and also depended on the level and quality of the qualifications held. For the most part engineers and technologists entered industry. Of the pure scientists, chemists were most oriented towards industry, so by 1971 66% of all chemists were employed in industry, 20% in schools or higher education and only 10% in local or national government or in research institutes; earth scientists, physicists and biologists, on the other hand, became decreasingly industry-oriented during this period. In the 1960s some British scientists went to the United States, constituting the "Brain Drain", which was, however, more the result of the seriously unsatisfied demand in the United States than of an over-supply in Britain. Industry must therefore be thought of, historically at least, as the prime employer of qualified scientists and engineers (QSEs), and in the English-speaking world by the end of the 1960s industrial demand for scientists and engineers who wanted to continue specialist work, at least initially, became less than the supply. Actual unemployment and even dismissal of scientists emerged as a new post-war phenomenon in the United States (but not in Japan) and many commentators began to talk and write about "over-production" of scientists.

Some recent British science graduates have undoubtedly suffered disappointment and some are, perhaps, enduring real hardship. There must be many young people now in the BSc, MSc, or PhD pipelines who are wondering whether they made the right decision at eighteen and twenty-one. They are not reassured by the Cassandra-like utterances of those modern windvanes of real or imaginary change, the university appointments boards officers, especially those from north of the River Trent. All concerned with this problem, whether they be employers, government, educational policy makers, university and polytechnic teachers or, last but not least, sixth formers themselves, need to give careful thought to the issues involved.

Demand for QSEs in Industry

The first question is clearly whether this phenomenon is temporary or is likely to persist. If it is the former, then there

Table 1 Percentage of Eighteen-year-olds Entering Full-time Higher Education

	Universities	Colleges of education	Advanced further education	Total
1955	3.2	2.0	0.5	5.7
1960	4.0	2.7	1.4	8.1
1967	6.0	4.8	3.2	14.0
1971	8.7	5.7	4.8	19.2

is little ground for change in our educational patterns except for that which rests on the need to improve for its own sake the educational experience which young people have in British higher education. I suspect that this diagnosis is incorrect. The signs are that industry will not wish to recruit highly trained but narrow specialists in the numbers likely to emerge from an unchanged higher educational system. Growth of research rather than development is unlikely to continue at the rate of the past two decades if only because many industries are made increasingly wary of innovation by the increasingly high costs and risks involved in development and marketing. Moreover, within the developed world national social priorities are changing, and as we move into the post-industrial society the growth of manufacturing industry may give place to greater growth in the service industries, reflecting desires for conservation of energy and raw materials, improvement of the quality of life and similar objectives. The science graduate will therefore have to enlarge his employment horizons. Many specialists will still be needed, but increasingly they will be working within multidisciplinary groups where their ability to communicate will be at a premium. The roles of individuals may also be expected to change more frequently; even in the 1960s it was the case that by the age of forty more than half the QSEs were engaged on work for which the detailed factual knowledge of first or second degree was thought by them to be of little consequence, either because it was outdated or because it was unnecessary. In my experience industrial QSEs, whether engaged in specialist scientific work or in management, technical service, sales, planning or any other of the multifarious duties they may be called on to perform, value much more highly the skills of logical analysis and an ability to apply these to new situations and of cogent verbal presentation of arguments to colleagues often less well equipped technically, together with more personal qualities of being able to cooperate fruitfully with others, often from different original disciplines, and the ability to gain the reciprocal cooperation of these colleagues.

University Lecturers

What of the employment prospects in the education sector? In the short term one must look to the White Paper on education[1] for guidance. The provision of nursery schools, the raising of the school leaving age, and the filling of vacancies for science teachers will provide employment opportunities for only a minute fraction of science graduates at the bachelor level. Institutions in higher education will, of course, continue to need able people at the PhD and higher levels, but in view of the slightly declining portion of science students in universities, the displacement downwards of staff/student ratios, and the often far from buoyant numbers of would-be science entrants to polytechnics, it is idle to pretend that recruitment in this sector will in the next decade approach the high levels of the mid-1960s.

It is also proper to ask whether the aspirations about university life of many would-be lecturers are likely to be fulfilled to the same degree as in the recent past. Many will wonder about their chances of unfettered choice of research and of securing the necessary financial resources. The government has stated in its White Paper on research and development[2] (Command 5046, para. 54) that it "attaches great importance to the support which all the research councils give to the universities and the new arrangements are designed to ensure that this should continue unimpeded". This statement must be taken literally, but "unimpeded" should not be read as "unchanged". The research councils are rightly considering, in the light of the quinquennial settlement, how best to assist in maintaining university research at the highest international level. Recent policies concerning selectivity will be reviewed and priorities will change; the role of postgraduate students may well be rescrutinized and attempts will have to be made to discover what validity attaches to the oft-repeated view that

involvement of a teacher in original research is essential if his teaching is not to be "stale, flat and unprofitable". But by and large the British university lecturer may in the 1970s expect his opportunities to do worthwhile research to be undiminished, even though he may increasingly do it cooperatively with colleagues from the same or other institutions and make use of national or international facilities and of trained research assistants rather than of so many research students, and he must be prepared to respond to mild external stimuli from the research councils or from government departments. As John Stuart Mill might have said, "His liberty will be the privilege of self-discipline".

If, however, his research role is to be little affected, the lecturer and his colleagues should expect to do some hard rethinking about their teaching. In view of the changed career expectancy of science graduates to which I have already referred, he will need to ponder how many of his students he should subject to a curriculum designed, as it is at present, primarily to produce a competent specialist researcher and what new educational single or multiple-subject programmes he should devise and encourage his other students to take.

Hortatory Comments

The twenty thousand or so scientists, engineers, medicos and so on on the staff of British universities are an unusually able group and exert a critical influence on the intellectual and personal development of the more gifted of our young people. Although the rate of recruitment of new staff will not match that of the 1960s, those appointed may look forward to an interesting and rewarding career in research and teaching, but collectively they will need to be more innovative than their predecessors because the career prospects of their students will be more diverse. In this connexion I would conclude with two comments which I believe to be of considerable importance. First, the lecturer should not allow his enthusiasm for his subject to diminish and he should aim to transmit that enthusiasm to his students. But in his teaching he should also remember that the most useful things he can give to his students are those habits of thought to which I have referred and which will be of permanent value in the students' subsequent career. He should impart to his students the conviction that the experimental sciences can be an excellent preparation for many careers, for they involve a unique blend of numeracy and literacy, of appreciation of the importance of accurate observation, of induction and deduction, of model building and model testing, of logic and of judgment which all of us, whatever our careers, have cause to use repeatedly. It follows that if science graduates can match in conversability and communicability their arts contemporaries it is the latter who will have to fear the competition of the scientists as these increasingly penetrate the traditional employment preserves of the arts graduates. The university lecturers will therefore have to think hard about the learning process of their own students and how to modify the curriculum content and pedagogy to improve the chances of his student acquiring or strengthening these desirable qualities.

Second, if our society is to be successful, both it and its individual members must be flexible and able to adapt rapidly to new opportunities and situations. This will in turn increase the number of reorientations which graduates will need to make in their careers. They will need help in their retraining and the universities and polytechnics are the obvious means of providing this help. But to be effective they will need to draw on the knowledge of industry and on resources which are additional to those which the University Grants Committee is now able to provide and university staff should be giving urgent attention to the best ways of carrying out this task.

[1] *Education: A Framework for Expansion*, Cmnd 5174 (HMSO, 1972).
[2] *Framework for Government Research and Development*, Cmnd 5046, para. 54 (HMSO, 1972).

Tentative Prognosis of Future Demand

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Higher education in science should never be specifically for employment, but if it can retain its educative function, while taking some cognizance of the possible shape of the market for its products, the frustrations and disappointments suffered by so many individual science graduates during the past few years may be somewhat lessened in future.

THE abrupt fall in the demand for QSEs (the accepted abbreviation for "qualified scientists, technologists and engineers") which occurred in Britain at about the beginning of 1971 is now a matter of history, and statistics are available which indicate its severity. The number of QSEs declared redundant during the past two or three years can only be guessed at, but that other sensitive indicator of demand, the total recruitment of science, technology and engineering graduates at BSc, MSc, or PhD levels to British manufacturing industry for first employment after graduation, is known to have been about 8,000 in both 1968–69 and 1969–70, but in 1970–71 it fell sharply to 6,500. If one omits the relatively stable categories of building, contracting, civil engineering, public utilities, the National Coal Board (NCB) and the United Kingdom Atomic Energy Authority (UKAEA), whose demands for graduates were fairly steady over the three years, then for oil, chemical, engineering and "other manufacturing" industries the drop was from 6,300 to 4,650—a fall of more than 25%. Figures for 1971–72, relating to the position at December 31, 1972, of those who graduated between October 1, 1971, and September 30, 1972, are not yet available, but indications are that they will not be significantly higher than those for 1970–71. When the first occupational destinations of 1973 graduates are collected by university careers and appointments services in the autumn and winter of 1973–74, it seems likely that these will show a recovery in recruiting figures to a point perhaps half-way back to the level reached in 1968–70. Within this more hopeful overall picture, however, there are still black spots in chemical industry (except pharmaceuticals), oil and mechanical engineering, and in heavy electrical industry where the demand for power engineers remains very low indeed. The computer industry, after an even more abrupt "stop", seems to be returning to the "go" phase as an employer of fresh graduates, although at a much lower level than in earlier boom years. Demand is strongest from light electrical industry, including applied physics, with GEC's requirement, for example, increased from about 400 graduates in 1972 to 700 this year.

All this is simple enough stuff, but of practically no use except to 1973 graduates wanting to know something about their personal prospects in the job hunt now in progress. Looking ahead even to 1974 is difficult, and from 1975 onwards, as Blaug has recently suggested, the process of manpower demand forecasting becomes so chancy as to be intellectually disreputable. But 1975 graduates are now first-year students in universities committed to their subjects, 1976 graduates have already made their choice in the form of applications submitted to the University Central Council on Admissions (UCCA) and the first generation of uncommitted students cannot therefore graduate before 1977 or reach what now seems to be accepted as full professional level as a working scientist or technologist (a PhD degree or something like three years of other relevant postgraduate training or experience) before 1980. If these latter students ask now about their employment prospects they must be given an answer of some sort, which itself must be based on a view of the longer term trends. This, for what it is worth, is one man's view of these trends.

Partial Recovery

It seems now to be agreed that, for manufacturing industry at least, the heady days of the early to mid-1960s graduate recruitment programmes are unlikely to return. Demand will recover, but to a lower level. Economies of scale have been operating in capital-intensive and graduate-intensive industries like chemicals, oil, electric power, steel and computers, and future recruitment levels in these industries will relate more to the replacement than to the augmentation of technical staff. For example, the overall effect of spending £3,000 million in the steel industry will be minus 50,000 jobs, and it is expected that organizations such as Imperial Chemical Industries (ICI) and Shell, whose contribution to growth is still large, will employ fewer staff of all kinds in the 1980s than they do today, even after the streamlining and heavy redundancies of the past two or three years. Within the overall reduction of 10 to 20% in complements the proportion of graduates may rise, but programmes of job enrichment, job enlargement and management development will continue to destroy jobs at all levels, not only those at the lower levels of skill. So, too, while inflation lasts, will the need continue for control of wage and salary costs.

Perhaps most significant for the scientist or technologist is the death in recent years of the assumption that more and better research and development lead almost inevitably to growth, national or institutional. It has been destroyed by the spectacular bankruptcy of Rolls-Royce, the demolition of the "spin off" argument as an economic justification for research and the relative rundown, partly at least on sheer cost grounds, of aerospace programmes in the United States and elsewhere. Defence programmes will no doubt get more expensive, but will not need proportionately more qualified staff.

All of these elements in the analysis of the supply and demand position are long term rather than short term in nature.

Even when, for example, the chemical industry re-enters a phase of high investment, perhaps two or three years hence, it would be naive to expect the creation of substantial numbers of extra jobs for chemists or chemical engineers. To attribute the problems of the past two years primarily to lack of economic growth is to be absurdly over-optimistic.

Other Employers

Manufacturing industry is far from being the only employer of QSEs. In 1968, according to the Department of Trade and Industry, there were in all nearly 350,000 economically active QSEs (185,000 technologists and engineers and 162,000 scientists) of whom 43% of the engineers and only 25% of the scientists were employed in manufacturing industry. Education was a larger employer of scientists (36%) with government and research (11%) being the only other significant employer except for "other" at 10%. Large numbers of engineers were employed in public utilities (11%), local authorities and construction (12%) and government and research (8%), with only 7% in education. It looks very doubtful whether government and research as an employer of scientists can be expected to increase its demand in the next few years, for neither the Scientific Civil Service nor the UKAEA is exactly a growth area, and "public utilities and construction" may be very hard put to it to absorb its quota of the large number of potential professional engineers already in the pipeline. Recent calculations by Head[1] about civil engineers suggest particular difficulties there in what has hitherto been a firm market. The ability of higher education to absorb its own products is on the wane, with a heavy age bias of existing staffs towards the lower end and a limited expansion of university and polytechnic science and technology departments envisaged in the White Paper[2]. Only something like 1 to 2% of today's university science graduates can expect to enter university lecturing jobs, and the equivalent departments in polytechnics and other institutions of higher education can expand no faster than the supply of students studying science in the sixth forms of secondary schools. Even that apparently insatiable market, science teaching in schools, is already visibly tightening and, apart from local pockets which may remain, the phrase "shortage of science teachers" will pass out of the language within two or three years. Headmasters and headmistresses advertising their vacancies can already testify to the startling change in sentiment in this market.

Although the longer-term effects of Britain in Europe, in terms of QSEs, are hard to forecast, it seems clear that in the developed part of the English-speaking world, with the minor exception of a small and temporarily unsatisfied market in South Africa, the same conditions of apparent oversupply exist; and in the developing countries the attitude towards expatriates and towards western science and technology has changed so much in recent years that no substantial market for the export of British QSEs exists there. No resurgence of the brain drain can be expected.

So prospects for the science graduate wishing to be employed as a scientist look relatively poor, statistically speaking, during the next 5 to 7 years. He can hope for a slow recovery of traditional demand, but my own view, expressed at a conference in 1971, that "this is the first of the seven lean years" was more optimistic than that of Professor R. V. Jones at the same conference, who thought that it would be the late 1980s to early 1990s before specific demand had again fully caught up with supply.

Where Will They Go ?

Two mechanisms are available to mop up "surplus" science and technology graduates who are not employable in their professional contexts. The first is the rapid takeover by graduates of technician-level jobs, a transition which has been in progress since the early 1960s. For example, statistics show an increase of 11,700 QSEs employed in manufacturing industry in 1968 by comparison with 1965, but they also show an increase of 11,750 in the number of QSEs employed as "technicians and technical supporting staff"—a very remarkable 1 : 1 ratio. But such a takeover provokes some pointed questions about the best method of educating and training technicians—namely whether this should be by university or CNAA degree course, by the old-style HNC or by today's HND, full-time or sandwich. It is by no means certain that employers would vote in favour of the university degree for this purpose.

The second mechanism is by the entry of QSEs into first occupations in which their specific knowledge and training are of little, or even of no, direct significance. This is not necessarily a matter for regret. *The Long Term Demand for Scientific Manpower*[3], published in 1961, had this to say on the subject. "In our view the possibility that there will be a surplus of scientists over immediate demands for employment should be welcomed. It should make possible a rational, as opposed to an emergency, use of the scientific disciplines. It should mean that at long last we shall have a supply of qualified manpower with a scientific training for management, administration, and the professions generally, in addition to those who up to the present have been drawn inevitably into vocational employment. We do not doubt that scientific education will adjust itself to this new prospect; and that in the same way as only a proportion of those trained in the classics and history have expected to find employment in their own fields of study, an increasing proportion of those trained in specialized scientific disciplines will obtain employment outside them. We think that both science and the nation will benefit from this adjustment."

This opportunity for "both science and the nation" is now with us as a continuing situation. No longer need the science graduate feel that he ought not to seek quite different employment, for example, in social work, accountancy, librarianship, non-scientific government service, banking or the retail trade; the skills he has acquired can now be looked at by him and by potential employers in a much less circumscribed manner. Even academic staff are slowly taking this point. And his skills may prove an unexpectedly marketable commodity; for example, the number of science and engineering graduates entering chartered accountancy articles today is increasing fast, but apparently at the expense of pure arts graduates, fewer of whom are now entering this occupation. But the very size of this movement of graduates away from first employment of "relevant" type—with, for example, up to 40% of chemistry graduates (and according to one source something like 70% of chemical engineering graduates) currently entering "non-relevant" jobs—makes it necessary to re-examine the nature and assumptions of scientific education at universities. Pippard's proposals some years ago of a framework of very general science courses for two years, as a preliminary to specialized study of a single subject at the equivalent of honours degree level, made great sense then but makes even greater sense now. If the BSc (or the Diploma in Higher Education, DipHE) could be taken in two years, and could include a liberal scattering of non-science courses, only those wanting and expecting to be employed later in their scientific discipline —perhaps 50% of the total entry—would specifically need to go on to the next two years of specialized study. The others could be offered the alternative of further broad courses, but not of a lower level, as a prelude to non-scientific employment. Under such a system choices of course having some significance for a future career could be made at a later age than is the case at present, and closer to the point in time at which employment decisions can no longer be postponed.

[1] Head C. R., *Surveyor*, CXLI (January 12 and 19, 1973).
[2] *Education: A Framework for Expansion*, Cmnd 5174 (HMSO, 1972).
[3] *The Long Term Demand for Scientific Manpower*, Cmnd 1490 (HMSO, 1961).

Trends in Employment of Graduate Scientists

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> In the past few years the most striking change has been the reduction in the number of first degree graduates entering employment and the increase in the number opting for teacher training.

IF graduate employment statistics had been collected in the Middle Ages, they would doubtless have shown that theologians went largely into jobs where their theological studies were directly relevant. More generally, the relationship between subject of study and job would have been direct and predictable.

Few arts graduates today would expect to "use their subject" on leaving a university, unless they had decided to teach. Until recently, most scientists could assume that they would be able to continue to work in jobs in which their scientific knowledge and training were directly relevant.

For the past two or three years, however, that has not been the case. It ceased to be true for chemists rather earlier than for physicists, and there were other differences in the speed of the change between the different scientific disciplines, but as a generalization scientists are now in a position little different from that which has long faced arts graduates. They may enter jobs in which their subject is of practical, professional value, but the likelihood is that they will not.

Tables 1 and 2 present the picture, and indicate how great some of the changes have been, particularly for the first degree science graduates. The total numbers entering employment on graduating have fallen, whereas the numbers embarking on teacher training have risen. Even more significant are the changes in the types of work to which those entering employment have gone. Research and development, scientific support and services to management, general training and line management, all show substantial reductions. Financial work has attracted many more scientists, and so has social work (though the total numbers are small).

The fact that biologists and chemists have been facing difficulties if they wished to work in their subject has been well publicized but, as Table 1 shows, the fall in the proportion of those taking specifically scientific work (other than teaching) is even more startling in the case of the mathematicians and the physicists.

Table 2, relating to higher degree graduates, shows a different balance, but essentially tells the same story. Research and development, with fewer openings, has drawn more on those with postgraduate qualifications than on first degree graduates. Even so, more higher degree graduates entering industry have taken up line management, rather than purely scientific, jobs.

These figures reflect sharp reductions in demand from the euphoric 1960s, as Holloway suggests in his article on page 378 of this issue. To say that there are fewer "science" jobs, and therefore that more scientists are going, and will go, into jobs where their science is a general educational rather than a specifically vocational qualification, though true, is not, how-

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Table 1 Statistics of British First Degree Science Graduates

First destination	1969	1970	1971
Academic study home	3,390	3,557	3,436
Academic study overseas	188	130	95
Teacher training	1,848	1,914	2,279
Social work training	24	17	21
Other training	688	767	741
Employment home permanent	} 5,150	} 4,866	4,405
Employment home temporary			392
Employment overseas	388	411	352
Other categories	1,868	2,198	2,324
Total	13,544	13,860	14,045

Type of work			
Scientific research and development	1,184	979	768
Scientific support and services to management	1,893	1,756	1,289
General training and line management	804	818	651
Financial work	206	270	605
Social work	26	36	81
Teaching and lecturing	331	273	338
Professional training	589	539	489
Other categories	217	195	184
Total	5,150	4,866	4,405

Proportion taking scientific work outside teaching	%	%	%
Biology and medicine	22.3	18.9	19.0
Chemistry	24.3	22.2	15.1
Mathematics and statistics	35.5	31.9	17.7
Geology and environmental science	14.2	17.3	15.1
Physics	31.4	29.1	19.5
Combined courses	22.3	20.6	14.2
All scientists	26.4	23.7	17.4

Table 2 Statistics of British Higher Degree Science Graduates

First destination	1969	1970	1971
Academic study home	618	666	734
Academic study overseas	394	326	254
Teacher training	32	31	50
Social work training			3
Other training	16	21	34
Employment home permanent	} 1,451	} 1,509	1,583
Employment home temporary			47
Employment overseas	310	332	299
Other categories	1,309	1,470	1,648
Total	4,130	4,355	4,652

Type of work			
Scientific research and development	725	753	756
Scientific support and services to management	204	250	235
General training and line management	53	56	126
Financial work	5	15	15
Social work	2	3	7
Teaching and lecturing	425	394	396
Professional training	5	12	25
Other categories	32	26	23
Total	1,451	1,509	1,583

Proportion taking scientific work outside teaching	%	%	%
Biology and medicine	17.0	17.1	19.8
Chemistry	27.4	29.2	24.9
Mathematics and statistics	22.1	28.9	18.5
Geology and environmental science	18.8	17.9	16.9
Physics	23.3	23.4	22.5
Combined courses	30.0	18.7	14.3
All scientists	22.6	23.3	21.0

ever, the whole truth. Other factors must be taken into account.

These include, notably, the changing attitudes of employers and of science graduates themselves, and the nature of employment in an age of rapid technological change.

In the case of attitudes, there is frequently a pendulum effect. From a policy of seeking as many scientists as could be persuaded to apply, industry has tended to turn to a policy of questioning their value to the organization in any numbers. Almost inevitably, such questioning produces exaggeration but it is surely intrinsically healthy. Recruitment should never take place unless a real need has been established and real prospects can be offered.

Graduates themselves similarly show exaggerated reactions, which are perfectly understandable. If industry ceases to woo them, and indeed questions their desirability, they will naturally tend to look for other suitors. Professional qualifications have an obvious attraction, and financial work, for which they may be well suited, still offers opportunities to obtain them.

The changing nature of employment presents rather more fundamental problems. Scientists who decide to become chartered accountants, or marketing men, or librarians, are consciously leaving their science behind them (except as an extremely useful base). Even those who enter employment where their scientific skills have provided the *entrée*, however, must now recognize that the speed of technological development may well render those skills obsolete before they have completed their working life (indeed, probably will do so). They may continue to work as scientists but work will be punctuated by the need to relearn and refresh themselves, to move in directions which they could hardly have foreseen on emerging from the university or polytechnic.

This brings one back to attitudes. Scientists are no longer in the position of the mediaeval theologians. They have moved from that position of happy certainty far more brusquely than the theologians had to do, but for those who can contemplate the new reality as one of hope rather than disaster, the prospect is by no means unpleasing.

Planning for Changed Expectations

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> In solving their own employment problems, scientists will ensure that they serve society in new ways.

THERE are now 350,000 qualified scientists and engineers (QSEs) in Britain, alongside a population of 550,000 who have reached a similar level of further education outside science. At present, the annual output of 15,000 scientists and 10,000 engineers is showing no sign of increase, and we seem to be heading for a state of affairs around the years 2000 to 2020 in which there will be a population of about 1 million QSEs and about 4 million other highly educated people in Britain. If science and engineering regain popularity, their proportion of the total will increase. Further education is undoubtedly going to be given to more than 20% of each age group by the early 1980s, so we are moving very rapidly away from a society in which further education was for people who would (as of right) enlighten and command about twenty times as many less educated and, hopefully, admiring contemporaries. Instead, the graduates will now have to do much more of the world's work themselves.

New Model

If one wishes to perpetuate the old "command" model (and I, for one, do not), then of course we are overproducing graduates. There is no possibility of having this number of centurions with no centuries to look after, and avoiding trouble. If, however, one takes the view that a boss-and-minion society can be replaced by something more cooperative and participative, then we are not producing too many highly educated people and can do with more, provided that planning is sensible and that people are told what to expect. Few would accept the observation currently to be seen painted on a shelter on Hampstead Heath: "All exercise of authority perverts: all submission to authority humiliates", but we must

listen with a lot of sympathy to our children's strictures on our structures.

Before tackling the current problem of careers for scientists, one must take a longer look at the coming decades. I am not speaking for industry, or ICI, or the Science Research Council, or even for my generation: I am speaking for myself. We must begin by going beyond the Robbins justification[1] for educating so many people in general and scientists in particular. We only have experience of three kinds of workable economy. The first is an authoritarian and stable system in which most people are forced to accept their lot, as in the ancient civilizations and in mediaeval Europe. The second, which eventually undermines the first, is a reformist, self-help system driven by a desire to escape from poverty and disease, as in nineteenth century England. The third, a natural development of the second, is a largely affluent system driven by a desire to grow in affluence, as is the case in Western nations now. None of these three systems needs mass advanced education, but those who are educated will perceive soonest that neither the second nor the third can continue indefinitely. In due course, overcrowding, aggression, and resource problems become dominant, and produce results that outweigh the advantage of further conventional advance. At this stage, which is certainly in sight, one either has to return to the first, authoritarian, non-growth system (to which the necessary meritocracy will be strongly hostile) or devise a growth system that generates a range of desirable activities which are neither productive of aggression nor demanding of resources other than human energy. Aldous Huxley, in *Brave New World*, described a prime example: a game entitled "centrifugal bumble-puppy". The range could include the writing and reading of poetry or literature, the composing and performance of music, or the painting and contemplation of pictures. If it includes cooking, it will have to be *haute cuisine*, and must not generate obesity. It cannot encompass the performance of services such as sweeping and cleaning, because these activities will inevitably be made unnecessary or improved in productivity (thus employing fewer) in an affluent society.

The factor commonly required for these permissible elements

in the ultimate growth economy is education. One key reason for this is that it will aid acceptance of the idea that population must be stabilized. Even more important, it provides a basis for understanding and demanding more music (performing and hearing) and more poetry (writing as well as reading), all of which can satisfy competitive urges. Sport will play a key part, but success in sport cannot be universal and its utility is therefore self-limiting. Only education can provide unlimited channels for acceptable cupidity, acquisitiveness and avarice. Alongside poetry and music can be set thought-intensive science. To discover pulsars, one needs equipment, but it is necessary to escape from the tyranny of programmed but basically foolish computers. Consequently, a big programme of discovery could involve an army of people obtaining satisfaction from the output of one big dish or one incessantly bleeping satellite telescope assembly: some would be trying out models of cosmic dynamics, and some would be poring over digital or photographic outputs. But computers would be used sparingly and intelligently. Intelligence-intensive biology would take its place alongside this intelligence-intensive cosmology.

The food, clothing, communications apparatus, permitted vehicles, and dwellings for this population would be produced by a small proportion of the work force, whose resource-winning and recycle procedures would be driven by solar photons, fixed in various ways. And a branch of this water-drawing and wood-hewing supertechnological fraternity would be preserving health for as long as mental capability lasted, edging life spans cautiously upwards but not so as to increase the population of mental and geriatric hospitals—and, with success, chipping back birth rates. There would be a strong link between these medical managers and the biologists in the "permitted growth" sector.

With such a pragmatic Utopia (and there really are not many workable alternatives other than much nastier tyrannies accompanied by periodic war and famine), there are plenty of careers for scientists: but chiefly for scientists with a keen perception of the limitations within which they may work. Because of the crucial importance of this acceptance of constraint, scientists will have to be strongly social animals, with broad perceptions.

Short Term Needs and Opportunities

The 1973–80 career question for scientists, and our future educational programmes, can only be looked at sensibly in terms of pictures such as that just painted or better alternatives. Many of the more immediate occupational patterns must be temporary, and one does not want a succession of disappointments, following the current dismay and discomfort arising from the fulfilment of Sir Michael Swann's largely unheeded prophecies of the mid-1960s[2]. The following points seem to be germane.

● The educational sector will saturate quite soon with scientists needed for teaching specialist science, whether at school or elsewhere. Thereafter, as the science teaching population will be young, wastage by retirement will be small, and the intake of specialist teachers will also be small. But there will be golden opportunities for more science to be included in general education, and for new arts and skills to develop in the vital business of spreading scientific awareness through the whole population.

● The science-based industries, whose costs are rising fast and whose technologies are becoming mature in many (but not all) areas, must improve the productivity of their scientists and managers, as indeed they must improve all productivity. To keep their age structure, costs, and promotion prospects reasonable, they should seek to maintain an intake of new graduates by encouraging some of those in the age range 25 to 35 to move into smaller companies who are their suppliers and customers, taking relevant skills with them. (Engineers have always done this.) But even with this measure, intake will be only a modest proportion of that during the 1960s. It will be vital to face all these problems, and pay in such a way as to make this sort of career pattern attractive.

● Public sector science will employ more scientists in and alongside administration, in particular in matters concerning the environment and trade. But standards will be high, and numbers only modest.

● The service industries (public and private sector) will increasingly employ scientists who are prepared to make initially dull jobs interesting—ranging from hospital management through waste disposal to transport logistics and economics. All of these subjects have tended to be regarded as humdrum, and to be treated as not specially worthy of good thinking and logic. All have, more recently, been greatly enriched by combinations of operations research and imaginative technology.

● The whole field of first-level management now involves a difficult mixture of the understanding of people, equipment, and systems. The traditional training of the "on the job" foreman is increasingly inadequate, although many foremen impressively succeed in educating themselves informally. Graduates will be needed as supervisors in many new types of plant, and this will account for quite rapidly growing numbers.

● Marketing does not have a glamorous intellectual image; at its dullest, it involves routine visits and, at its least scrupulous, it can involve misrepresentation. Yet assisting people to discover their real needs, and then filling them, is skilled and of vital importance both to the customer and the whole process of innovation. Good profits can only be earned by making products that are appreciably nearer true needs than most other products—whether these discovered needs require new formulations, new chemistry, different engineering, or altered materials. Good graduates, encouraged to use their skills, can transform a market, and larger numbers will almost certainly be so employed.

● The professions (law and accountancy, for example) are receiving a bigger input of science graduates. This too is to be welcomed: a cost accountant who understands science is likely to bring a fresh approach and to be able to help a manager to ask for performance numbers and norms that will concentrate on essentials: more important, he will find it easier to stop collecting and displaying numbers that are useless because of irrelevance or inaccuracy. The proportion of scientists in these classes could become substantial.

The exploration of these new opportunities has to be done chiefly by the job-hunting graduate himself: employers are not usually over-anxious to change their sources of staff without persuasion. Consequently, graduates need help and encouragement to knock on new kinds of door and to know what to say when the door is opened an inch or two. Supervisors can help in this and some special exercises such as the SRC's one-week courses, principally run by the Careers Research and Advisory Centre (CRAC), can further embolden. Graduates in America have been employed more widely for many years now, and American experience is well worth scrutiny.

Science graduates, then, have to become more closely involved with society for two reasons. The first, and more immediate, is to help provide goods and services more efficiently, thus creating leisure. The second is to help society to use this leisure without using too many resources, making the place unpleasant to live in, or increasing disturbance and neurosis. In solving their own employment problems, scientists will be getting their skills used more fruitfully than ever before.

[1] *Report of the Committee on Higher Education (Robbins Report)*, Cmnd 2154 (HMSO, 1962).
[2] *The Flow into Employment of Scientists, Engineers and Technologists (Swann Report)*, paragraph 32, Cmnd 3541 (HMSO, 1968).

Employment of Graduates in Physics

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Although the employment prospects for physicists in industry may improve in some cases in the next few years, medical physics and accountancy, banking and commerce may well be new growth areas.

IN considering the present and future employment prospects for graduates in physics it is useful first to establish the demographic background. According to the best official estimates the number of economically active physics graduates increased from about 15,000 in 1959 to more than 30,000 in 1972. If the number of those graduating in physics each year remains constant this "stock" will rise to 40,000 by 1976. A small fall in new enrolments to physics departments will not seriously alter this short-term extrapolation.

The question arising from these figures is simply whether there has been and will be an increase in the number of jobs for physicists to match the increase in the numbers in the market for employment. In attempting to answer this question it is necessary from the outset to differentiate between employment which requires the specialist skills and knowledge of the physicist *pur sang* and employment for which a knowledge of physics is useful but not essential or, alternatively, where the intellectual discipline of the study of physics is a good foundation. One might call these "traditional" and "non-traditional", although the non-traditional type of employment has been significant since physics emerged as a separate university subject.

In the 1950s and most of the 1960s there was considerable expansion in the number of jobs of the traditional type both in industry and in higher education (arising from the growth of colleges of advanced technology and the new universities). By the end of the 1960s university expansion had virtually stopped and British industry was having to cope with great economic problems. It was at this time, some three years ago, that the job market for scientists and engineers changed from a seller's to a buyer's market.

Recent Trends

At this stage it would be useful to see what employment new physics graduates have been obtaining recently. The University Grants Committee (UGC) produces comprehensive statistics on the first employment of graduates but this is not published until the end of the following year, hence the figures for 1971 are the most recent from this source. These show that among first degree graduates about 30% went on to further study, about 15% went into teacher training and about 35% obtained permanent employment. The remainder were overseas graduates returning home, in other training and so on. Of those in permanent employment 18% were in public service (central and local government), 12% in education (at all levels), 50% in industry and 20% in commerce and other non-technical activities. Of higher degree graduates 20% were able to continue with research by means of, for example, post-doctoral fellowships while about 50% went into permanent employment;

of this latter category 10% were in public service, 30% in education (mostly universities), 40% in industry and the balance in commerce, etc.

A recent survey of the 1972 first degree graduates carried out by the Institute of Physics, to which about a third of the graduates replied, revealed that 37% were studying for a higher degree, 16% were undergoing teacher training and about 40% were in permanent employment, mostly in industry or public service. Of those in employment more than a third said they were in jobs which did not require their physics. Among all of those who had obtained a post, that is, employment and further education of all kinds, only a small percentage, however, said that they were not satisfied with their position. Perhaps it was too soon for disillusionment to have set in.

The starting salaries of those in employment, excluding further education and training, showed a considerable range but two-thirds of the salaries were between £1,200 and £1,600 a year. It is not known how job satisfaction correlates with salary.

It is a reasonable assumption that, in the short term at least, those who employ physicists now will continue to do so. In government service and higher education the situation seems to be quite straightforward although it should be remembered that many of the people in departments of engineering, particularly electrical engineering, metallurgy and others, have at least a first degree in physics.

It is, however, in industry that the greatest variety is probably shown. A recent analysis of the firms employing members of the Institute of Physics showed that by far the largest group of employers was the electrical and electronic industry, which accounts for something like 40% of the total. The chemical industry and general engineering were the next largest groups but each had less than 10% of the total. There was a wide spread of employment in other sectors but in all cases the numbers involved were small.

This survey did, of course, cover people who had been in employment for varying lengths of time and would therefore reflect the employment situation as it had been in past years. There is, however, career development with any one individual and it is important to look at this, for a new graduate should be interested not only in what job he is doing in his first years after graduation but what he might be doing ten or twenty years later. It has always been appreciated that a proportion of scientists who have entered industry to carry out research and development move away from this function into technical sales, production, marketing and general management. What was not known was the proportion of those starting in the research and development department (which virtually all scientists did) who moved into other departments and the time scale of the movement.

Changing Expectations

These questions were looked into some four years ago as part of a larger investigation on the relationship between education in physics and the needs of industry. The employment of physicists in twenty or so large companies was looked at in detail and overall it was found that some 40% were employed in non-research and development work. Examining the age distribution showed that for the under 25 age group there

were twice as many in the research and development function as elsewhere. This ratio fell with increasing age until in the 43–50 age group there were more in non-research and development work. It was notable but not unremarkable that those not in research and development were the better paid.

This investigation showed that even five or six years ago the young physics graduate, and his employer, were beginning to realize that it was worthwhile to move out of research and development at an early age rather than to accept this move as an unfortunate necessity when one became too old for research. On the contrary it was found to be a satisfying and rewarding experience. The extension from moving after a year or two in research and development to going straight into non-research activities after graduation was even then apparent.

This transition from "traditional" to "non-traditional" work is well established but it has not usually been a sharp one. In many cases it has been a question of doing a "non-traditional" job in association with active scientists in an industry using science and/or engineering. The time scale of the transition seems to have shortened in recent years but the environment has not been completely unfamiliar, not to say alien, to the physicist.

The new phenomenon is the turning of physicists to "non-traditional" jobs in a "non-traditional" environment. It should be said at once that individual examples of this have occurred for a very long time, most particularly during the economic depression of the late 1920s and early 1930s—a period which has obvious parallels with the present day. The surveys quoted above show that a significant number of new graduates are now going directly into accountancy, banking and commerce, and these numbers will undoubtedly grow in the future.

This movement into the legal and commercial field is by no means restricted to physicists. Figures quoted in the latest annual report of Imperial College showed that between 1965 and 1971 the proportion of all first degree graduates of the college going into these fields increased from 3.1% to 13.1%

and for those with a higher degree from 0.8% to 10.9%. In addition graduates in the arts, humanities and social sciences are also becoming increasingly interested in these fields of employment.

There is much evidence to show that a study of physics forms a good basis for the subsequent study and practice of many other subjects. It is reflected in the fact that more than 90% of those who take physics at A-level do not subsequently specialize in physics, in the fact that many of those with a first degree in physics go on to do a higher degree in another subject and in the fact that many who start out as physicists achieve success in other fields.

Opportunities in the Future

Where does all this lead to in considering the job opportunities and future careers of those who will graduate in physics in the next few years ? It seems quite evident that although there will be many "traditional" jobs physicists will have to look increasingly to "non-traditional" areas for employment. In the traditional fields the overall picture does not seem to be one of appreciable expansion, but there may, nevertheless, be limited areas of growth. Medical physics could well be one such area. In industry an improved economic climate will increase the number of jobs but these are more likely to be in production and technical support functions rather than in research and development.

This increasing orientation towards non-traditional employment has to be accepted by the student long before he graduates. It is important that the student's expectations should be realistic and it is now no longer realistic for somebody studying physics to be sure of making a career as a physicist. Of course the high flyers, who are also really dedicated to research or teaching, will continue in traditional paths but the others must accept that their study of physics has been an education, preparing them for many possible careers rather than a vocational training preparing them for only one possible career.

Prospects for Graduating Chemists in 1973

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> The Secretary of the Royal Institute of Chemistry traces the trends in the employment of graduate chemists.

A FEW years ago no one would have been interested in an article of this kind, for it went without saying throughout the 1950s and most of the 1960s that a degree in chemistry was a passport to a secure and interesting job. Indeed the situation for nearly twenty-five years after the end of the Second World War was such that chemistry graduates rarely had to make any effort to find a job because the employers came to them. It was not so in the 1930s and it is not so now; the inevitable question is: are we again in a situation like that of the 1930s? I believe that the answer is clearly no and that the situation today is totally different from what it was between the wars.

In the first place the present situation is a dynamic one— which it was certainly not in the thirties—and as the American sociologist Alvin Toffler has so vividly pointed out in his book *Future Shock*[1] the rate of change and the rate of diversification

in Western society are both increasing with frightening rapidity. Certainly if the number of chemistry graduates in 1971 (the last year for which figures are available) had been the same as it was in 1965—1,731—no one would have had any difficulty in finding a job. In fact, the number of graduates in 1971 was 2,457 and 196 of these were still seeking employment at December 31 in that year (Tables 1 and 2). Table 1 shows that the growth in the number of chemistry graduates has been considerable in the past fifteen years and even though

Table 1 Numbers of First-degree Chemistry Graduates

1958	1,130	1962	1,391	1966	1,967	1970	2,514
1959	1,179	1963	1,431	1967	2,034	1971	2,457
1960	1,418	1964	1,547	1968	2,564		
1961	1,387	1965	1,731	1969	2,679		

The figures do not include CNAA graduates or graduates of the Royal Institute of Chemistry (230 and 358 respectively in 1971) as the patterns of first employment of these graduates are not recorded. It is very unlikely, however, that this exclusion affects the argument developed.

Table 2 Principal Destinations of First-degree Chemistry Graduates as at December 31 of Each Year

Year	Research or academic study (Britain)	Teacher training	Employment in Britain	Seeking permanent employment	Unknown	Total No. of graduates
1968	873	300	1,052	97	87	2,564
1969	877	310	1,061	100	157	2,679
1970	850	319	913	140	145	2,514
1971	764	405	774	196	135	2,457

there has been a decline since 1969 the number graduating in 1971 was still much higher than that in 1958. This, of course, is a result of the principle adopted by the Robbins Committee and followed by successive governments that the number of university places should aim to meet the demand from suitably qualified school-leavers—and not the demand from potential employers. A rate of growth of this magnitude —significantly in excess of the rate of growth of the economy —had of necessity to lead to a situation where supply of graduates exceeded demand and the crunch came for chemists in 1970. It came also in other Western countries at about the same time—or, in some cases, is coming now—and the employment prospects for newly graduated chemists are worse than they are here in, for example, the United States and the Netherlands.

Profits and Employment

The essential reason why the crunch came in 1970 is that this was the year in which large-scale science-based industry, and particularly the chemical industry, started getting into difficulties from world-wide over-capacity and greatly intensified international competition. Seeing its profit margins being rapidly eroded, industry reacted by cutting back on its most expensive raw material, labour, and this included scientists. Although many arguments can be advanced to show that this was a short-sighted policy in terms of the future vitality and innovative capacity of industry it is frankly difficult to see what different decisions anyone could have taken in the circumstances. The result was the mounting unemployment figures, and chemists were no more immune than any other salaried professionals. Indeed, in some ways they were more vulnerable, for their activities do not normally have any direct and immediate effect on profitability.

It is worth examining the figures for industrial employment in some detail, as these provide the key to the whole problem. Table 3 shows that in 1971 only 465 of the 2,457 graduates with first degrees entered private or nationalized industry— about 19%, the proportion having dropped sharply from 31% in 1969. To these figures must be added the number of graduates with higher degrees entering industry; Tables 4 and 5 show that these were 303 and 286 in 1969 and 1971 respectively. (Table 4 also shows, incidentally, that higher-degree graduates in chemistry have not so far been affected by unemployment and this is borne out by surveys of PhD graduates carried out by the Royal Institute of Chemistry for the Committee of Heads of University Chemistry Departments —including a survey of 1972 PhD graduates.) Expressed as a

proportion of those leaving university, either with a first degree or a higher degree, the total number going into industry in Britain dropped from 44% in 1969 to 30% in 1971 (1,129 out of 2,570 in 1969 and 751 out of 2,526 in 1971). This is a substantial drop—and it probably went further in 1972 —but it affects less than half of chemistry graduates and it might be thought surprising that it should have such a far-reaching effect. Why, in fact, do the opportunities in the other areas of employment not expand to take up the slack?

The reason, ultimately, is that industry (with commerce) is the only wealth-producing activity in our society and every other activity—education, government research or whatever— must be paid for out of the taxes levied on this created wealth, either by corporate taxation of the company or individual taxation of its employees. The total employment situation is therefore always sensitive to the health of industry and although governments can cushion the effects of an industrial recession for a time they are powerless to do so for long. It is essentially for this reason that government research, which is a traditional area of employment for chemistry graduates, has been cut back during the past few years and is not now in a position to take up any of the slack.

The other traditional area of employment for chemists is teaching and here the intake into schoolteaching, either directly or through teacher training, has shown a marked increase (Tables 2 and 3). There is evidence that this trend continued in 1972, over 10% of PhD graduates entering schoolteaching in that year, and it is very welcome after so many years of inadequate numbers of well-qualified chemistry schoolteachers.

In further and higher education, on the other hand, and particularly in the latter, the expansion in the 1960s was so rapid that we are now inevitably in a period of consolidation and there is very limited opportunity here. Indeed the age structure of chemistry staff in the universities is such that the number of vacancies is likely to be about 4% of the total staff for some years to come—even on the somewhat optimistic assumption that the opportunity is not taken to reduce the establishment of a department when a member of staff leaves.

With the possible exception of schoolteaching, there is then little hope of any early increase in the numbers of vacancies in the areas of employment that are the traditional alternatives to industry for chemistry graduates. What of industry itself? Here the position is brighter. The output of the United States chemical industry broke all records in 1972 and that year has been described as one of the most spectacular in the industry's history. There is little doubt that the chemical industry in Britain has also "bottomed out" and is starting to move up again, and the same is true of other large science-based indus-

Table 3 Principal Categories of First Employment in Britain of First-degree Chemistry Graduates

Year	Public service	Teaching	Oil, chemical and allied industries	Engineering and allied industries	Other manufacturing industries	Nationalized industries and the UKAEA	Accountancy, banking, insurance and other commerce	Total No. going into British employment
1968	75	63	453	140	175	58	51	1,052
1969	66	65	451	154	167	54	65	1,061
1970	53	60	389	119	124	56	74	913
1971	98	88	234	58	117	56	95	774

Table 4 Principal Destinations of Higher-degree Chemistry Graduates as at December 31 of Each Year

Year	Research or academic study (Britain)	Postdoctoral fellowships	Overseas students returned home	Employment in Britain	Seeking permanent employment	Unknown	Total No. of graduates
1968	91	304	107	410	16	67	1,159
1969	93	270	104	463	14	73	1,235
1970	100	230	128	472	15	97	1,247
1971	88	219	108	463	19	122	1,245

tries. Although the upturn is more obvious in terms of the financial health of companies than in any immediate increase in recruiting, the latter must follow soon. The general trend in all employment in Britain is strongly upward and this also must influence the position for chemists, for the outstanding characteristic of changes in employment level is that they produce a snowball effect, either upwards or downwards.

The only real doubt is whether the upturn will come in time to help the 1973 graduates and this must be a matter of speculation. Perhaps all that can be said is that the situation for chemistry graduates in 1973 will be no worse than in 1972 and could well be significantly better; and there will almost certainly be a substantial improvement in 1974 and 1975, especially as the number of chemistry graduates will continue to fall in this period (the number admitted into chemistry courses having fallen every year from 3,308 in 1967 to 2,526 in 1972).

Given that the employment prospects for chemistry graduates in industry will shortly begin to improve—if they have not already done so—there remains the question of what types of employment there will be. There is a growing consensus of view that there will be no return to the situation where large numbers of chemists are recruited into the research and development function, and this has perhaps been put most clearly by Duncan Davies in his 1972 address to the Royal Society on discontinuities in chemistry and chemical technology. He sees the growth areas for employment of chemists in industry as outside the traditional research and development function and this view is supported by a preliminary statistical model for the chemical industry prepared by the Department of Trade and Industry. The model, which is admittedly based on very simple assumptions, predicts for the period 1973–81 that the density of professionally qualified scientists and engineers (QSEs) in research and development will not increase and therefore that the absolute numbers will increase only if there is an increase in total employment in the industry; that the number of QSEs in associate professional (that is, technician) roles will increase at the same rate as between 1965 and 1968; and that the density of QSEs in professional functions outside research and development (production, commerce, and common services including top management) will increase at the same rate as between 1965 and 1968.

Whether these predictions are quantitatively accurate or not, there can be little doubt of their qualitative correctness. It has been officially estimated that by the year 2000 the number of graduates produced annually in all disciplines will be twice

as great as the number of what would now be regarded as "graduate jobs". Diversification of employment for graduates must therefore take place more and more, and this will require greater adaptability by graduates in subjects like chemistry, which have hitherto been regarded as vocational, than by graduates in arts or social sciences. Furthermore, the diversification will not be confined to industrial employment. Already there is a significant increase in the number of chemistry graduates entering commerce (from 51 in 1968 to 95 in 1971; Table 3) and this trend will certainly continue. Many other areas of potential employment for graduate chemists spring to mind and notable among these is the administrative Civil Service. The point has already been made that the adequacy of government funds depends on the success of industry and commerce in creating the necessary wealth. But the allocation of priorities for government spending is a political decision and political decisions are strongly dependent on advice from senior civil servants. The more scientists there are in such positions therefore, the more likely is it that science and technology will receive their fair share of public resources. This is even more important at the present time, when the image of science has taken a beating in practically all Western countries.

To quote Duncan Davies, "It is possible and correct to meet the new situation with a series of campaigns to secure the employment of many of those trained in science in activities for which technological capability is highly desirable, but where it has hitherto been absent". He believes that chemistry is "a subject that uses concepts and numbers in even balance . . . and that additionally has much central relevance, so that there is a good argument for according it a place as a central enabling subject, alongside languages and mathematics".

Here then is a challenge for any chemistry graduate worth his salt. There will continue to be the traditional jobs in research and development and in teaching, but these will form a decreasing proportion of the total; at the same time there will be a growing number of other jobs in a wide variety of different fields and many of these will provide exciting opportunities. As with all jobs, they will ultimately be what the chemist makes of them.

The figures in the tables are taken from the annual University Grants Committee publication *First Employment of University Graduates*, and I acknowledge permission to reproduce them.

[1] Toffler, A., *Future Shock* (Bodley Head, 1970).

Table 5 Principal Categories of First Employment in Britain of Higher-degree Chemistry Graduates

Year	Public service	Teaching	Oil, chemical and allied industries	Engineering and allied industries	Other manufacturing industries	Nationalized industries and the UKAEA	Accountancy, banking, insurance and other commerce	Total No. going into British employment
1968	34	132	149	15	40	24	2	410
1969	32	103	217	30	40	16	7	463
1970	14	110	237	35	45	16	4	472
1971	41	115	197	33	41	15	7	463

Careers for Biology Graduates

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The Secretary of the Institute of Biology suggests that environmental work, not necessarily of a strictly biological nature, will attract more British biology graduates in the years to come.

BEFORE 1939 the great majority of biologists were teachers, chiefly in schools, with only a few centres outside the universities, such as Kew Gardens and the Natural History Museum, employing research workers. The Second World War, however, changed the pattern: biologists were deployed in pest control, malaria eradication, penicillin production, the development of radar and operational research. After the war the growth in the numbers graduating in biological subjects kept pace with the demands from industry, the research councils and the expanding universities, and there was an approximate balance between demand and supply until about 1970. Throughout the twenty post-war years the only sector in which there was a serious shortage of biologists was school teaching.

By 1970 the output of biologists from universities was three times that of 1960 ; the numbers entering various types of employment each year from 1959 to 1971 are shown by Fig. 1. The most recent information about the numbers of qualified biologists in various types of employment is given by the 10% sample census made by the Registrar General in 1966 (see Table 1). (Unfortunately the figures from the 1971 census are not yet available.)

Because those considering careers in biology either for themselves or their pupils will have recent or current experience of the situation in schools, there is less need to describe the work of teachers even though those in schools are the largest single group of biologists. At A-level the move to replace the separate subjects of botany and zoology by biology is likely to continue and, if accompanied by a growth in physical science as an A-level subject, could provide well balanced courses for both intending scientists and those wanting a broader education. At lower levels there will be less emphasis on "biology" as a subject with the moves toward integrated science or environmental studies. Hence those attracted to teaching will have opportunities for innovation. The existence of Biology Teachers' Centres and the activities

Table 1 Employment of Biologists in 1966

University teachers	2,185
School and college teachers	6,940
Research work	3,250
Administration/management	940
Technician/industrial worker	1,210
Other	1,695
Total	16,175
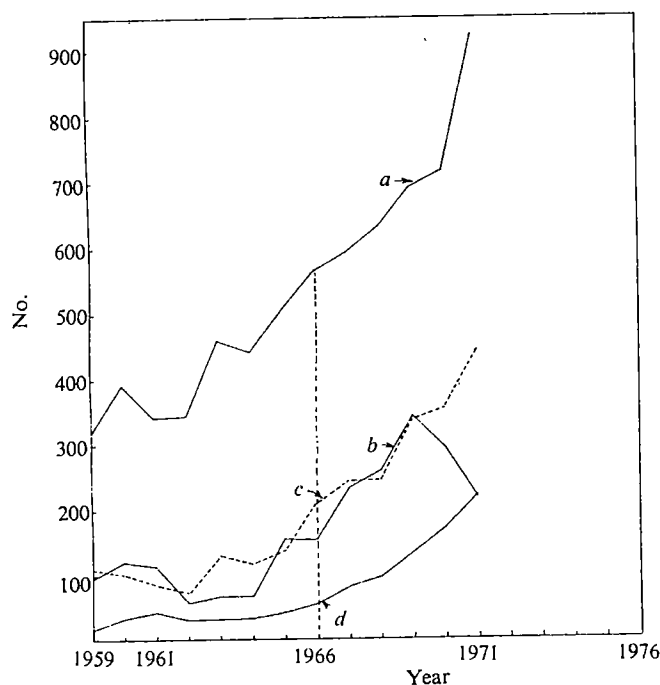
of the local branches of the Institute of Biology should enable teachers to overcome any feelings of isolation and help them to keep up to date in their chosen subject.

Posts in the Civil Service and research councils will be available for those who have higher degrees or a good first degree, but recruitment will be principally for replacement, not expansion. When the reorganization of support for government research and development has been completed, which may well not be until the spring of 1974, there could be a number of vacancies for work on new projects. There should be vacancies in the National Health Service when the recommendations by the Zuckerman Committee for a unified scientific service are implemented. Although the largest group of biologists in the NHS will remain that of biochemists, the numbers of microbiologists, immunologists, physiologists and geneticists are growing.

Recruitment by industrial firms has been low recently but there are signs of economic recovery. If this occurs then the food, pharmaceutical and agricultural industries will once again be seeking biologists for research, development and administration. Several companies are developing biological processes for the production of synthetic protein ; another possible development is the large-scale extraction of protein from leaves ; a few companies already have biologists working on the production of conventional vegetables by tissue culture.

The increasing awareness of the environmental problems arising from the growth of the human population and its

Fig. 1 First employment of biologists with first degrees or equivalent qualifications. a, Education; b, manufacturing; c, government; d, other sectors.

increasing demands for energy and resources ought to lead to the employment of more biologists in the fields of reproductive physiology and biochemistry and on the effects of pollution on living systems. The establishment of Regional Water Authorities in England and Wales will lead to a greater use of chemical and biological knowledge in the management of water resources, and the Royal Commission on Environmental Pollution is at present considering the training desirable for those who will be employed in environmental work at various levels. More biology graduates could well enter the fields of landscape architecture, planning and resource management: they should be prepared to take specialist training so as to become fully qualified in the appropriate profession.

If the numbers entering biological courses at universities and polytechnics remain at the present levels the total population of those with a degree in a biological subject will double

in the next ten years. There is no possibility that the number of posts in teaching and research will grow in proportion and thus many of those obtaining a biological degree must be prepared to consider it as an education but not necessarily a training for specific work in the field of biology. Because they will have become accustomed to dealing with such things as complex systems, variability, the interrelations of organisms and behaviour, biology graduates should be well equipped for posts in management and administration. Those with the level of numeracy now developed by many modern courses in biology will be suited for work in systems analysis and operational research. Those who do not go into research or teaching but into the administrative civil service, information work, industrial management or local government should find satisfaction in work which taxes their intellect even if it does not draw directly on the detailed knowledge acquired in a university course.

Employment of Science Graduates in Australia

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The Careers and Appointments Officer and the Academic Registrar of the Australian National University discuss the problems faced by the science graduate in Australia. One of the difficulties is that comprehensive statistics have only recently become available.

AUSTRALIA has a small population and a correspondingly small university enrolment, so one might reasonably expect that a clear picture, statistical and otherwise, could easily be drawn of the output and the employment of science graduates. Unfortunately this is not the case. Even in terms of measuring output, it is difficult to give a precise figure, because of differences of nomenclature and course organization in the universities. It is clear, however, that of the 15,000 bachelor degrees conferred by Australian universities in 1971, approximately 3,000 were in pure or applied science (including such areas as agricultural science, but excluding specifically professional qualifications such as veterinary science).

We can be rather more precise about the output of PhD graduates, for the fields of study are usually more clearly defined. Of the 750 PhD degrees awarded in 1972, approximately 450 were in science and in applied science[1].

Outputs at both the first degree and the PhD levels increased spectacularly during the 1960s. In 1961 the total of all bachelor degrees conferred in Australia was less than 5,000 (15,000 in 1971) and the total number of PhD degrees conferred rose from 174 in 1963 to 750 at present. Particularly in the case of the PhD this increase resulted in large part from a conscious effort to increase both the quantity and the quality of postgraduate training in Australia. The PhD is a relatively new degree, the first having been awarded in 1948, and when the Murray committee[2] looked at Australian universities in 1957 it saw a great need to provide highly qualified manpower to staff the universities in the predictable boom of the 1960s. The Murray committee, and others in the early 1960s, were

confident that the new outpouring of highly qualified people in the sciences could be absorbed[3].

By the mid-1960s, thoughtful observers had begun to question the capacity of Australia's economy and workforce to absorb the large number of science graduates, amongst others, particularly as the needs of tertiary education itself began to be met[4,5]. At the beginning of the 1970s there is in Australia a graduate employment problem which affects science graduates, although it is not apparently as serious as that which exists in some other countries.

Employment of First-degree Science Graduates

1972 was the first year in which Australia-wide statistics were collected of the destinations of first-degree graduates. Table 1 provides some relevant information from this collection.

We do not have comprehensive figures for previous years which can provide a basis for comparison, although this will be the case in the future. Earlier surveys have been carried out, particularly by appointments services in individual universities, and there have also been special studies of particular subject areas[7-12]. The available data provide something of a picture of the employment of science graduates, at least as far as their first destinations are concerned, but there is little information about their later careers.

The figures for 1972, given in Table 1, do enable us to make concrete certain generalizations which have been aired frequently. Perhaps most important is the fact that a very small percentage of first-degree graduates in science find their way, initially at least, into private industry. Some further comment about employer attitudes will be made in the discussion on PhD graduates. It is also possible to suggest that the traditional first degree in a pure science discipline has not produced graduates who are particularly interested in, or well trained for, industrial applications of science.

Some other general impressions have to remain just that, although they would be agreed on by most people in the appointments field. Many science graduates are finding, and will continue to find, great difficulty in locating a first job

Table 1 Destinations of Selected First-degree Science Graduates in Australia, 1972

First destination	Physical sciences %	Bio-logical sciences %	Earth and environ-mental sciences * %	Agri-cultural science and forestry %	Mathe-matics † %
			Chief field of study		
Higher degree studies	28	28	16	13	14
Teaching and teacher training	34	29	46	15	39
Other further study	7	9	4	4	9
Public service and other government employment	9	13	11	43	15
Private industry and commerce	10	4	12	8	10
University employment	7	7	3	3	5
Other	5	10	8	14	8

Based on data gathered for the Graduate Careers Council of Australia and appearing in ref. 6. The information relates only to degrees granted by universities. Applied science is excluded because the original tabulation amalgamated applied science and engineering graduates.

* Includes graduates in geography.

† Includes graduates from faculties of arts and so on with mathematics as the principal subject studied.

which is "in science", and this is usually their preference. As the notion of the professional scientist comes almost exclusively to mean someone with a PhD, many BSc graduates will be forced out of the job market in specialist fields, particularly research, and must see themselves as non-specialists. The teaching profession will perhaps begin to find its needs for science teachers met, after years of inadequate supply.

There are changes taking place, affecting first-degree science training, which have a crucial importance for employment. There are moves towards inter-disciplinary courses, one example being a human studies programme at the Australian National University. There is an increasing number of specialist postgraduate courses, whether for diplomas or master's degrees, which can provide a vocational capstone to a first-degree education in science. It is possible now to do such courses in education, librarianship, computing, administration and environmental science. It is very likely that, for many BSc graduates to fit happily into the workforce outside academic and research establishments, an even wider variety of such courses, with industrial applications, needs to be provided. Already, as Table 1 indicates, most BSc graduates feel the need to supplement their first degrees with some sort of further training. It is clear that the BSc is not a professional degree nor a job training.

Another significant change is the increased availability of courses in the applied sciences, both within the universities themselves and in the rapidly expanding colleges of advanced education. The existence of these courses, both in the traditional technological fields and in newer areas such as in environmental science, will have an important bearing on the employment of pure science graduates who stop at the BSc stage. If it is obvious that only a minority of those now undertaking pure science degrees will be able to work in pure science, the question must be asked whether a training in some applied area will be more appropriate for many. The role of the first degree in pure science other than as preparation for research careers should perhaps be the subject of healthy questioning. An examination of the factors relating to the employment of first-degree science graduates done with the same depth and thoroughness as the Academy of Science study of PhD graduates mentioned below would be most useful.

Employment of PhDs

The pattern of employment of PhD scientists in Australia has been examined more closely in recent years, particularly in some disciplines. The numbers of graduates are fewer, the PhD is more professionally focused than any first degree and the traditional avenues of employment are fewer. But, just as for the first degree, reliable information is in relatively short supply and no Australia-wide figures giving details of employment are available.

What is clear is that in the early 1970s the production of PhD scientists in most fields exceeds the capacity of the academic labour market to absorb new staff. As the PhD is seen primarily as a professional preparation for those entering university teaching or full-time research work, employment problems inevitably ensue. Stories of 100 or 150 applications for university posts abound and epitomize the situation —a vastly increased number of PhDs chasing a few academic jobs. This situation is familiar in all English-speaking countries.

It must be remembered that the PhD is very recent in Australia and that the number of awards quadrupled in the 1960s. The urgent needs of the universities themselves have been met, as have those of government-supported research (particularly through the Commonwealth Scientific and Industrial Research Organization, CSIRO). A stage of reassessment now seems to have been reached, when it is difficult for some PhD graduates to get jobs and when there is some evidence that students are unwilling to enrol for PhDs as knowledge of these difficulties becomes publicized (sometimes inaccurately). Again, the precise extent of these changes has not been recorded and at the moment it is only an educated guess that the rate of increase in the enrolment for the PhD has fallen.

Some reasons for employment difficulties are clear, such as the flow-on effect of similar difficulties in other countries, and the levelling off of university growth within Australia. There has been a continuing debate about the level of participation by Australian PhD graduates in industrial research and development and in non-scientific employment. What is certain is that Australian industry tends overall to enjoy a fairly low level of investment, of both finance and manpower, in research and it has consequently been difficult for the initial "overflow" of PhD scientists to be absorbed into jobs in industry which they prefer. Added to this is the simple novelty of the idea that there are PhD graduates looking for jobs outside education and research.

From the mid-1960s on, there has been a number of studies of the factors affecting the supply and demand situation for PhDs. Armstrong, Hill and Ross[4] foresaw the "overflow" problem. Parker et al.[13] and Middleton et al.[14] have examined the situation of PhD chemists in detail. West[15,16] has looked at the general question of the use of scientific manpower, and has linked this to a consideration of a national science policy, an area which is relatively untouched in Australia. The Commonwealth government now has a Department of Science, and scientific manpower questions are part of that department's concern; for the moment, however, the valuable work done by those mentioned and others still adds up to a rather piecemeal picture.

Recently the Standing Committee on Science and Education of the Science and Industry Forum of the Australian Academy of Science has received a report[17] which makes a more comprehensive attempt at understanding attitudes towards PhD training and employment in Australia. The study, as did several earlier ones, focuses on chemists; it also contains a comprehensive review of relevant previous studies and writings in Australia. The importance of chemistry in the PhD picture can be seen from Table 2, which gives a breakdown of PhDs awarded in science in 1972.

The Academy of Science study looks very closely at the nature of PhD training in science in Australia, at the general problems of understanding the market for highly qualified

scientists and at the attitudes which exist amongst students towards the employment market. It is clear that the often-assumed prejudice against employment in industry and in non-tertiary teaching does exist and that many PhD students themselves (more than 40%) are worried about employment prospects. The definition of "professionalism" which students have absorbed throughout their careers virtually requires that

Table 2 Australian PhD Degrees in Science in 1972*

	% of total
Applied science	9
Biological science	16
Chemistry .	56
Physics	11
Geology	4
Mathematics	4

* Compiled from material supplied by the Bureau of Census and Statistics.

they work within a university environment for professional fulfilment.

This report, thorough as it is, in a sense simply points the way to a need for an even more searching investigation of the relationships between PhD study and employment. We know there are problems of overflow from the traditional areas of employment and difficulties in gaining acceptance, on both sides, of the employability of PhD graduates in industry. We do not know the precise dimensions of the problem. In 1973, for the first time, the Graduate Careers Council of Australia will attempt to collect information for PhD graduates as it does for first-degree graduates, indicating not only the pattern of their first destination but also the extent of unemployment and underemployment. Just how this information, together with other data, will be used by students, university planners and employers remains to be seen. In the meantime it can simply be said that Australian PhD scientists can face a real employment problem, given the nature of their training and the prevailing attitudes in the job market.

The Future

In Australia, graduates themselves have begun to show a deep interest in their prospects of employment. This interest is more likely to be articulated by smaller well-identified groups such as PhD graduates in chemistry or physics who will see themselves as professional groups. First-degree science graduates are a much more heterogeneous body and will see themselves much less clearly as a professional group or groups.

Consequently few initiatives have been taken by first-degree graduates to analyse and seek an understanding of their employment problems but a number of studies have been undertaken at the initiative of PhD graduates. Most of these studies have been limited to the examination of a particular professional group. Valuable as these limited studies are, it is essential that much more detailed and extensive studies be undertaken of education and employment in Australia for first-degree and higher-degree graduates. The graduates themselves must be encouraged to seek an understanding of their problems but this will not be enough; other bodies must also become increasingly active. Australia-wide studies of education and employment of science graduates at all levels at the depth of the studies prepared for the National Institutes of Health by the National Research Council of the United States[18-20] should be undertaken.

In a federation such as Australia, with difficulty in securing nationwide policies on education, we are doubtful about the possibility or the wisdom of the adoption of a central policy to regulate the supply of science graduates to the various outlets. There can, however, be no doubt that the days of

complete *laissez-faire* for universities in the choice of the areas into which they will put their effort to produce graduates (both with first degrees and higher degrees) are over. Increasingly universities will be persuaded and in some circumstances directed by government and government agencies using the power of financial control.

In our opinion, therefore, it will become vital for universities and government to have as much information as possible about the factors involved in the selection by students of university courses, the attitudes of universities in the offering of courses and the attitudes of employers in making use of the graduates from those courses. The more complete and reliable this information is, the less likely it is that there will be conflict between government, the universities and the employers.

There are some very good signs for the future. Government, particularly the Commonwealth government, has already asked the Australian Universities Committee to make a careful study, in collaboration with the departments concerned with labour, science and education, of the factors involved in determining the demand for particular types of graduates. The universities and the Australian Vice-chancellors' Committee, in collaboration with the Australian Academy of Science, have undertaken a deep and careful study of the education and employment of science PhDs and the Graduate Careers Council of Australia following a conference entitled "Graduates for What?", held in Canberra in August 1972, has received Commonwealth government support for a continuing survey of the first destinations of Australian university graduates. The appointments boards of Australian universities continue to use their limited reserves to conduct surveys of supply and demand for graduates.

It must be recognized that worthwhile studies would probe the question of the basic objectives of many university courses and may disturb many universities which are too ready to rely on tradition and hunch in the decisions they make concerning the continuation of their existing courses and the introduction of new ones.

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Stratigraphical Relationships of the Plio-Pleistocene Deposits, East Rudolf, Kenya

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This report summarizes the stratigraphical relationships of the Plio-Pleistocene sediments at East Rudolf and formalizes the stratigraphical nomenclature.

THE geological investigation of the area east of Lake Rudolf, northern Kenya, was initiated in 1969 by A. K. Behrensmeyer and continued by a team from Iowa State University in 1970, 1971 and 1972 as a part of the National Museums of Kenya expedition. This report summarizes the stratigraphical relationships established during the 1971 and 1972 seasons of the Plio-Pleistocene sediments and formalizes the stratigraphical nomenclature.

In 1968 the National Museums of Kenya, under the direction of R. E. F. Leakey, organized an expedition to the northeastern shore of Lake Rudolf. The purpose of the expedition was to determine the palaeontological potential of the sediments observed by Mr Leakey in an earlier aerial reconnaissance. Subsequent work has shown that the Plio-Pleistocene sediments did indeed contain fossils and to date more than eighty hominid fossils, a wealth of late Tertiary and Pleistocene mammalian fossils and a series of archaeological sites have been discovered.

The East Rudolf Basin is located at the northern end of the Gregory Rift Valley. The main graben forms the Suguta Valley at the southern end of Lake Rudolf and trends across the lake in a north-northeasterly direction. The northward continuation of the trend is the Kinu Sago fault belt east of Lake Rudolf and the Stephanie graben on the Ethiopian border[1] (see Fig. 1). The area studied lies on the northwestern flanks of this trend.

The Suregei cuesta forms the eastern margin of the East Rudolf Basin (see Fig. 2), and consists of a series of interbedded Miocene basalt flows, associated palaeosols and sediments which were uplifted and tilted westward by early Pliocene faulting. The basin is transected by the northeast-southwest trending Kokoi structure, which consists of Pliocene basalt flows and interbedded lacustrine sediments recently faulted and uplifted by northward trending faults. Faults in the area, although numerous near the lake, are of relatively minor importance; they form a series of small half-grabens and horsts with a general northward trend. Except for reversals caused by faulting, the sediments dip gently toward the lake.

Correlation

The sedimentary exposures in the East Rudolf Basin were originally separated into three areas because of the difficulty of stratigraphical correlation between them[3]. The exposures at Ileret, the northernmost area, are separated from those along the Koobi Fora ridge, the central area, by the Kokoi structure and a large Holocene alluvial plain complex to the east of the Kokoi. The Holocene floodplain deposits of the Laga Bura Hasuma separate the Kubi Algi area, the southernmost, from the Koobi Fora area (see Fig. 3).

During the 1971 and 1972 field seasons strata were measured and described along the western slope of the Suregei cuesta

at the eastern margin of the Ileret, Koobi Fora and Kubi Algi areas. Marker beds were established and traced around the Kokoi and the head of Laga Bura Hasuma into the previously described exposures at Ileret and Koobi Fora[3].

The oldest rocks exposed in the East Rudolf Basin are the basalt flows (11.6 ± 0.5 m.y. BP and 14.1 ± 1.4 m.y. BP)[3] of the Suregei cuesta. In the northern and central sequences a basal conglomerate consisting of basalt cobbles and pebbles in a pale yellow-brown claystone matrix non-conformably overlies the basalts. It grades laterally into a very pale orange laminated claystone which contains 5–8 m thick lenses of basalt boulders which range up to 1 m in diameter. A series of grey-orange, fine to coarse grained, crossbedded sandstones interbedded with three prominent grey tuff horizons conformably overlie the conglomerate and claystones. This entire sequence attains a composite thickness of 155–170 m. The lower portion is near-shore to transitional lacustrine grading upward into a dominantly fluvial sequence intercalated with thin transitional lacustrine beds.

The three tuff horizons are the best marker beds available and serve as the basis for correlating the Ileret, Koobi Fora and Kubi Algi sedimentary sequences. The lower, a complex— here designated the Suregei Tuff Complex—can be traced around the Kokoi along the western flanks of the Suregei cuesta. It extends from immediately east of the Ileret area to about 15 km to the south along the Suregei. The Suregei Tuff Complex can be used to correlate the strata measured at the northern end of this traverse with the strata measured at the
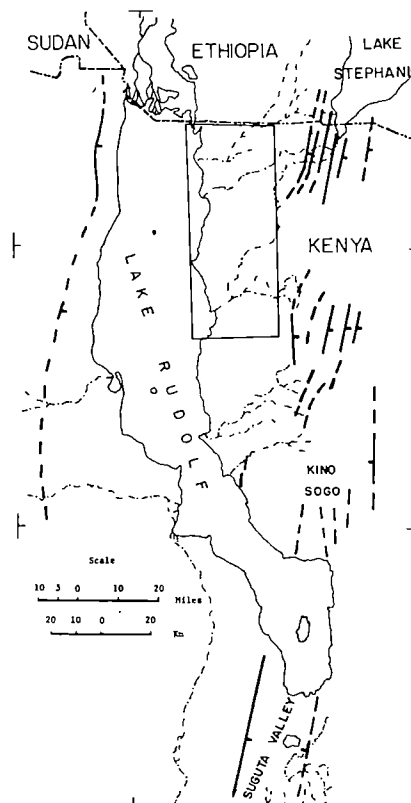
Fig. 1 Index map showing the location of study area and the boundary faults of the Kenya Rift.
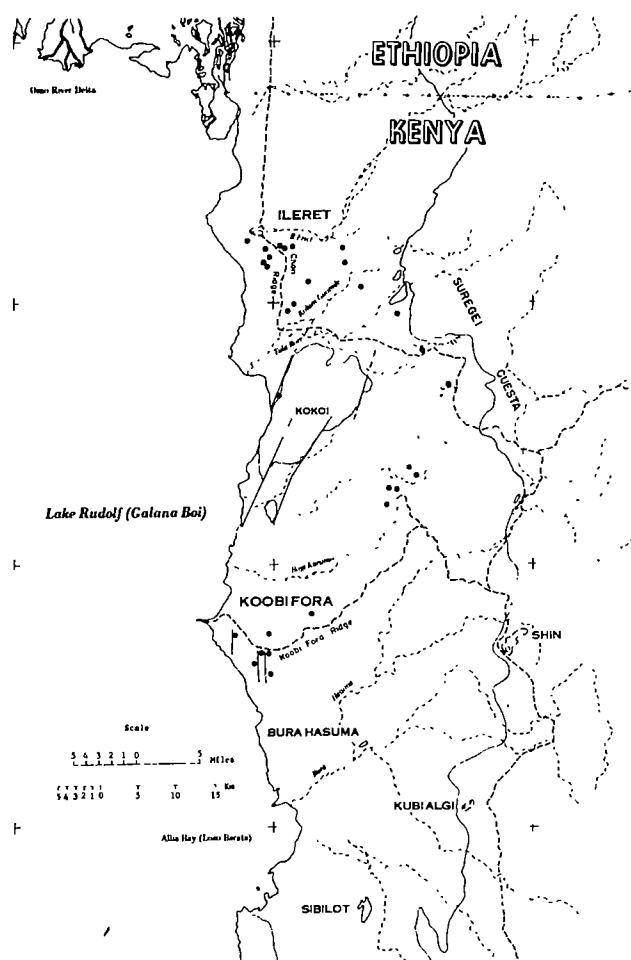
Fig. 2 Map of the study area showing prominent physiograph-
ical features and locations of sections.

southern end. The uppermost tuff in the sedimentary sequence
at the southern end of this traverse can then be traced along a
series of low NE–SW trending escarpments into the sedi-
mentary sequence in the Koobi Fora area. This tuff correlates
with the KBS Tuff in the Koobi Fora IIA unit of Behrens-
meyer[2] and Vondra et al.[3]. The sequence of tuffs is essentially
the same in the exposures in the Ileret area and those to the
south. The intervening strata and the vertical separation and
corresponding thicknesses of the tuffs are similar. On this
basis the uppermost tuff in the northern sequence has been
correlated with the uppermost tuff in the southern sequence
and with the KBS Tuff at Koobi Fora with confidence (Fig. 3).
The intermediate tuff is here named the Tulu Bor Tuff.

The KBS Tuff and associated strata can be traced south-
ward to the floodplain complex of the Laga Bura Hasuma.
The strata below the KBS Tuff are traceable around the
Laga Bura Hasuma to a series of ridges immediately south of
the floodplain complex of the stream. The exposures pre-
viously described by Vondra et al.[3] are then traceable along
a series of terraces into the lower portion of the sedimentary
sequence near Kubi Algi. The upper 80 m of these exposures
is similar in lithology and number of tuffs to the sedimentary
sequences exposed along the Suregei cuesta in the Ileret and
Koobi Fora areas. The first tuff below the KBS Tuff can be
correlated with the Tulu Bor Tuff and the next lower tuff
complex with the Suregei Tuff Complex (Fig. 3).

Nomenclature

With the correlation established it is now possible to forma-
lize the stratigraphical nomenclature. The term Koobi Fora
Formation is here proposed to include those sedimentary
strata which lie between the basal contact of the Suregei

Tuff Complex and the upper contact of the prominent tuff,
exposed along the Ileret ridge, here named the Chari Tuff,
or the basal contact of the Holocene grey, tuffaceous, pre-
dominantly lacustrine siltstones which represent a late stage
rise in the level of Lake Rudolf (Fig. 2). The exposures located
near Koobi Fora at 3° 56′ N latitude and 36° 15′ E longitude
(BH6136, East Africa Grid) best illustrate the lithology of the
formation and are here designated as the type exposures.
This includes the informal Koobi Fora I, II and III units of
Behrensmeyer[2] and Vondra et al.[3], and the lower unit at
Ileret as defined and described by Vondra et al.[3].

Those beds in the Ileret area formally designated the "lower
unit"[3] are a lithologically homogeneous sequence of fine
grained sandstones and siltstones. They are geographically
restricted to the Ileret ridge and as yet cannot be correlated
with the sequence at Koobi Fora. Therefore, the term Ileret
Member is proposed for the beds which lie between the upper
contact of the KBS Tuff in the Ileret area and the top of the
Chari Tuff which caps the Koobi Fora Formation. The
outcrops located in the Ileret area at 4° 16′ N latitude and 36°
15′ E longitude (BH6173, East Africa Grid) are designated
as the type exposure.

Informal member designation is applied to the Koobi
Fora Formation in the Koobi Fora area until the lateral
relationships in the upper part of the formation can be definitely
established. The lower portion of the formation between the
basal contact and the top of the KBS Tuff is designated as the
lower member and the strata above the KBS Tuff are referred
to as the upper member.

Those strata that lie below the basal contact of the Suregei
Tuff Complex are here designated as the Kubi Algi Formation.
The outcrops located along a terrace trending toward Kubi
Algi at 3° 45′ N latitude and 36° 19′ E longitude (BH6915,
East Africa Grid) are designated as the type exposure.

The Guomde Formation is proposed to include those
strata which lie between the top of the Chari Tuff on the
Ileret ridge and the overlying grey tuffaceous siltstones which
represent a late stage rise in the lake level. The upper contact
of the Guomde is marked by a 1 m thick tuff. The exposures
located on the Ileret ridge at 4° 18′ N latitude and 36° 15′ E
longitude (BH376, East Africa Grid) best illustrate the lithology
of the formation and are designated as the type section.
The Guomde Formation comprises the middle unit at Ileret
as described by Vondra et al.[3].

The term Galana Boi is retained for the grey, tuffaceous
siltstones which cap the Guomde Formation at Ileret and
applied to the fourth unit recognized in the Koobi Fora
area by Vondra et al.[3]. Although the lithology and strati-
graphical position are the same for the late stage lacustrine
beds at Ileret and Koobi Fora their exact lateral relationships
are not yet fully known.

The environments of deposition represented by the Kubi
Algi, Koobi Fora and Guomde Formation and the Galana
Boi beds are currently being worked out so that only a pre-
liminary summary of the palaeogeography can be presented.
Detailed lithological description and depositional history of
the units proposed along with aerial geological maps showing
their distribution will be published in the near future.

The sediments of the Kubi Algi and Koobi Fora formations
are interpreted to represent a prograding deltaic complex.
At the margins of the basin, thin lenses of near shore lacu-
strine sediments are intercalated with the predominantly deltaic
plain and fluvial deposits documenting periodic lacustrine
transgressions. The sediments tend to coarsen upward in the
centre of the basin indicating delta growth and regression
through time. Periodic coarsening, large-scale cut and fill
structures and angular relationships with underlying sediments
are characteristic of the basin margin fluvial deposits. These
features are attributed to the elevation of the source area and
downwarping of the lake basin as a result of periodic tectonic
activity along the rift system.

Mammalian fossils occur throughout the Kubi Algi and

Fig. 3 Stratigraphical sections illustrating correlation.
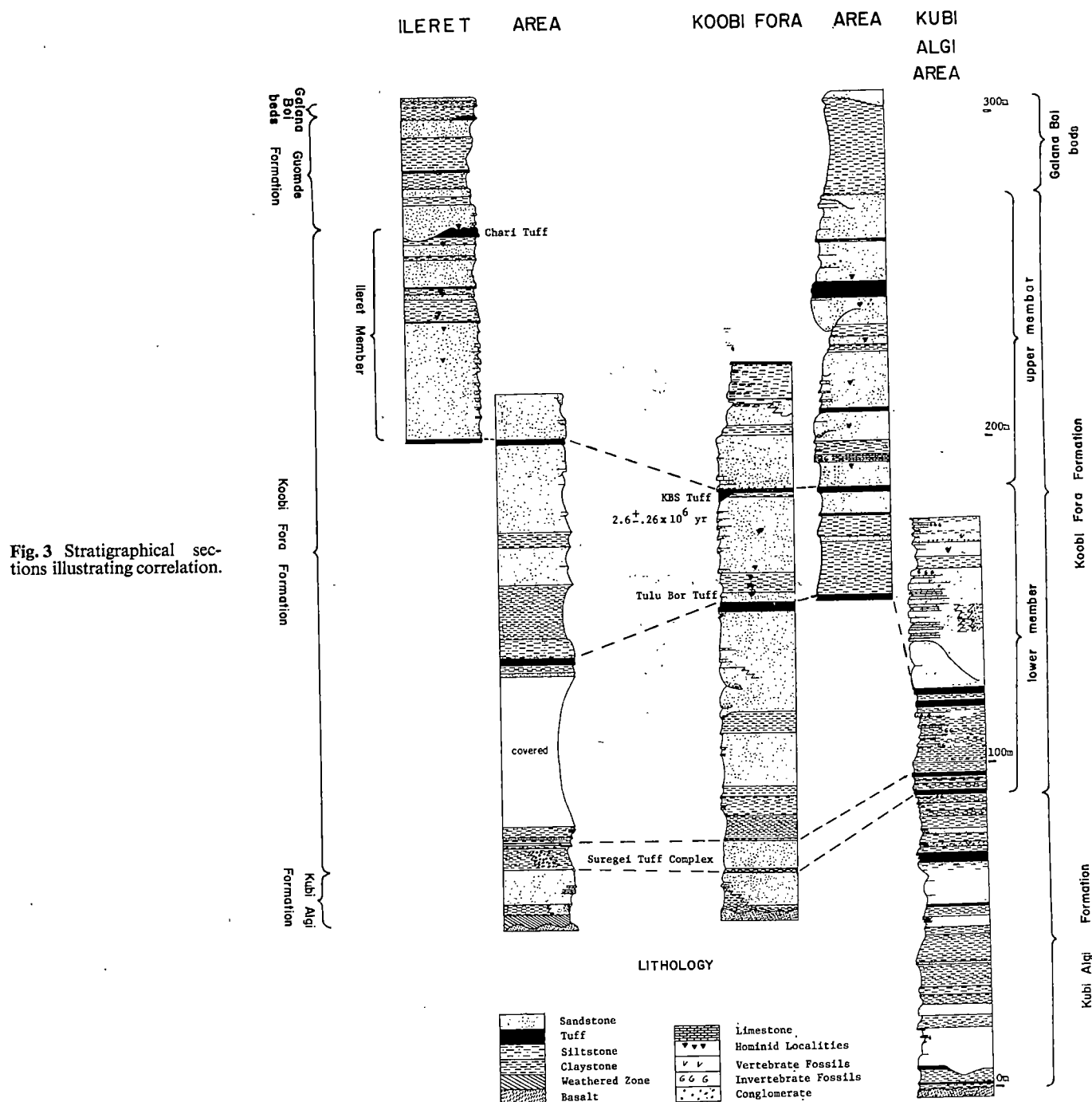
Koobi Fora formations, but an abundant representative sample is preserved only in the upper portion of the lower member and in the Ileret Member of the Koobi Fora Formation[6]. This sample is the basis for the faunal zonation of the Koobi Fora Formation[6]. Hominid fossils usually occur in the upper portion of the Koobi Fora Formation. The localities are indicated in Fig. 3. Hominid KNM-ER 1470, recently described by R. E. F. Leakey[7,8], was probably eroded from a sandstone of deltaic plain origin in the upper portion of the lower member of the Foobi Kora Formation, 35.5 m below the KBS Tuff.

The Guomde Formation, which overlies the Koobi Fora Formation with angular unconformity, represents a limited transgression of the lake in the Ileret area. The sediments were deposited predominantly in nearshore lacustrine and deltaic plain environments.

The Galana Boi beds, which unconformably overlie the Plio-Pleistocene sediments, range from coarse-grained fluvial deposits to fine-grained nearshore lacustrine silts. They occur up to 120 m above the present lake level. The sediments document both a major lacustrine transgression around 9,200 years BP and significant BP tectonic activity post-9,200 years.

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LETTERS TO NATURE

PHYSICAL SCIENCES

Redshift of OH471

THE purpose of this letter is to draw attention to the very high redshift, $z = 3.40$, of the QSO OH471.

The position and identification of the radio source OH471 were communicated to us by C. Hazard and are based on the accurate positional work of the group at the Royal Radar Establishment. The source had previously been identified by Gearhart, Lund, Frantz and Kraus[1] who also publish a finding chart. The position coordinates are

$$\alpha_{1950} = 06 \text{ h } 42 \text{ min } 52 \text{ s}$$
$$\delta_{1950} = +44° 54' 33''$$

On the Palomar Sky Survey the identification is a neutral, stellar object of estimated magnitude $m_B \sim 18$–18.5 mag.

The object has been studied spectroscopically with the Cassegrain image tube spectrograph at the Steward Observatory 90 inch telescope. Two spectrograms (SI 830a, 835a) have been obtained covering the range 3200–5800 Å at a dispersion of ~ 240 Å/mm. They both clearly show strong emission features at 4548 Å and 5351 Å, the former being somewhat weaker but broader than the latter. The ratio of measured wavelengths (1 : 1.177) agrees well with the rest wavelength ratio (1 : 1.176) of OVI λ1033.8 and Lα. Among strong emission lines normally observed in QSOs, no other ratio of rest wavelengths falls close to this value. We therefore tentatively identify the feature at 5351 Å with Lα and that at 4548 Å with OIV (1031.9, 1037.6) possibly blended with a contribution from Lβ. The redshift of OH471 would then be $z = 3.40$, substantially greater than the previous highest redshift $z = 2.88$ for 4C5.34 (ref. 2).

Although our redshift determination rests primarily on these two emission lines, the derived value of z is supported by the following additional evidence:

(i) According to Lynds[3] OVI is the dominant emission feature shortward of Lα in the spectrum of 4C5.34.

(ii) An emission feature at ~ 5460 Å seems both too strong and too wide to be attributed solely to the night sky Hg λ5461 line. It would, however, correspond to NV λ1240 at the derived redshift. A third spectrogram SI 840 covering the range λ5000–7200 Å at a dispersion of 180 Å/mm, although severely underexposed because of intermittent cloud, showed evidence of a weak emission feature near 6820 Å which would correspond to CIV λ1550 at the suggested redshift. Both of these lines, however, require confirmation.

(iii) The spectrum of OH471 is rich in absorption lines suggesting a high redshift, $z > 1.7$, say. If the feature at 5351 Å were identified with another, normally weak, line instead of with Lα, it would follow that emission Lα must be absent altogether from the spectrum. For example, SiIV λ1397 and HeII λ1640 have a wavelength ratio 1 : 1.174 and could therefore be identified with the observed emission features; the corresponding redshift would then be $z = 2.26$. The absence of strong features at 3966 Å and 5054 Å corresponding to Lα and CIV λ1550 respectively would then require explanation.

(iv) Although higher resolution spectrograms are required for a detailed analysis of the absorption line spectrum (an observational programme to this end is under way at Steward Observatory), one absorption system can probably be discerned on the well-widened spectrogram SI 835a. Strong, fairly broad, absorption features were found at 5281, 4225, 4126 Å and may be identified with Lα, Lγ and Lδ at a redshift z_A of 3.3440, 3.3444 and 3.3445 respectively. There is a broader, strong feature centred at 4462 Å which may be due to a blend of Lβ and a line (or lines) in another absorption system. Finally, there is a rather weaker blend centred at 4080 Å which may contain a contribution from Lε in the same system. Confirmation of this system must, however, await further spectroscopic evidence.

(v) The continuum of OH471 seems to decrease sharply shortward of ~ 4000 Å corresponding approximately to the redshifted wavelength of the Lyman limit (912 Å) in the emission system. Indeed both blue region spectrograms seem to be dominated by the night sky emission shortward of ~ 3900 Å, by contrast with spectra of other objects taken with the same system; this would be consistent with strong absorption in the Lyman continuum. Continuum distributions are, however, notoriously difficult to assess from photographic material and this point also requires confirmation using some form of linear detection system and proper sky subtraction.

On the basis of this additional evidence we feel that the line identifications and the consequent high redshift $z = 3.40$ are probably correct.

If QSO redshifts are due mainly to Hubble expansion OH471 is the most distant object so far known as well as being among the most intrinsically luminous. Its presence at $z = 3.40$ and $m_B \sim 18$–18.5 argues against explanations of the apparent paucity of QSOs with redshift exceeding 2.2 in terms of intergalactic obscuration at earlier epochs. The neutral colour does, however, raise the question of whether the redshift dependence of observed colour for a fixed intrinsic spectrum[4-6] introduces selection effects that work against discovery of high redshift objects[7]. With the extremely accurate radio positions now available (to which the identification of OH471 in a crowded star field bears ample testimony), this question can be settled observationally. There is, however, little evidence at present against the view expressed by Lynds and Wills[2] that the apparent dearth of high redshift QSOs is due to their intrinsic rarity.

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Hydrogen Flash in Stars

DURING the past few years there has been some progress in understanding the way in which a star approaches the main sequence. In their studies of the pre-main sequence evolution of stars, Ezer and Cameron[1] assumed that the stellar material started with the highest possible adiabat consistent with the virial theorem (for a given temperature a high adiabat has a low density and a low adiabat has a high density). In later hydrodynamic collapse studies of the formation of a star with zero angular momentum, Hayashi[2] and Larson[3] showed that much of the internal energy of the collapsing gas is radiated away, so that the stellar material must start on a much lower adiabat. The gas in the centre of such an object can only be heated by compression, so that it remains on a low adiabat. As the outer layers of the star fall onto this core, they undergo shock heating, due to gravitational potential energy release, which raises their adiabat, and allows the star to form a stable body in hydrostatic equilibrium prior to reaching the main sequence.

It is unrealistic to expect a star to form with zero angular momentum. Star formation studies[4] have shown that collapsing interstellar gas should form a flat disk, from which the star should form by gaseous dissipation processes[5]. The gas density near the disk centre is comparable to that in the collapsing core of Larson's models at which the first halt and mild shock heating occurs[3]. Hence shock heating effects should be relatively unimportant when a flat rotating disk (primitive solar nebula) is formed. The initial low adiabat of the gas in the disk will not be raised during the dissipation, but is likely to be substantially lowered as a result of radiation into space from the photosphere[5].

We have estimated the initial adiabat of the gas in the disk in several ways. Collapsing interstellar gas undergoes isothermal compression with a temperature of about 10 K as long as the emitted radiation is free to escape from the system[2,3]. When the density becomes high enough, the subsequent compression is adiabatic, but there is an ambiguity concerning the adiabat, because we do not know the distribution of the hydrogen molecules between the para and ortho forms[6]. We have used Larson's estimate of the temperature and density at which the switch from isothermal to adiabatic compression begins, and have computed the adiabat based on two possible limits in the relative number of parahydrogen and ortho-hydrogen molecules.

A third estimate is based on the pressure and temperature conditions deduced for the primitive solar nebula at the time of meteorite accumulation. Accumulation processes should take place rapidly in the primitive solar nebula[4], so that the thermodynamic conditions associated with accumulation probably differ rather little from those in the initial nebula. Although there is still considerable uncertainty associated with the meteoritic cosmothermometers and cosmobarometers[7–10], we can take approximately a temperature of 450 K and a pressure of 5×10^{-6} atmos as the conditions defining the adiabat.

We extended these adiabats toward higher temperatures and densities, taking into account the internal energy of excitation of hydrogen molecules, and the dissociation and ionization of hydrogen and helium. Because the adiabats are relatively low, thermal dissociation of hydrogen molecules is not complete before effects of pressure dissociation become important; we

have estimated the lowering of the dissociation energy at higher pressures following Vardya[11]. The subsequent thermal ionization of the hydrogen atoms is very inefficient; more than half of the hydrogen atoms remain neutral until pressure ionization takes place. At higher densities the ionization energy of hydrogen is lowered through coulomb binding of electrons to the plasma[12], but pressure ionization results chiefly from the partial shielding of the K-shell electrons in the neutral atoms by free electrons inside the classical Bohr radius[13]. The final adiabat is relatively insensitive to crude approximations in this treatment.

After ionization is complete, the adiabat can be written in the conventional form $P = K\rho^{5/3}$. With the pressure and density expressed in c.g.s. units, we found for our three estimates of the initial adiabat, $K = 1.08 \times 10^{13}$, 1.67×10^{13} and 2.61×10^{13}. The first two of these values correspond to the Larson estimate for the onset of adiabatic compression, the first when hydrogen molecules are all in the parahydrogen form, and the second when the para/ortho ratio is 1/3. The third value corresponds to meteoritic accumulation conditions. Because it represents the highest adiabat, our subsequent discussion is based on this third value.

We consider a star which has this initial adiabat everywhere in its interior structure. Such a star can be represented[14] by a polytrope of index 1.5. The central conditions are determined through specification of the total mass M and the adiabatic constant K. For the centre of such a polytrope we find a temperature of 7.0×10^7 K and a density of $7,200$ g cm^{-3}. These values are much higher than now exist at the centre of the Sun. For the present central solar temperature of 1.5×10^7 K, the density on the adiabat is 700 g cm^{-3}, also much higher than the present central density of the Sun. Further lowering of the adiabat by radiative cooling would increase these discrepancies.

So the Sun is unlikely to have formed as a spherically-symmetric body in hydrostatic equilibrium before the onset of hydrogen-burning at the centre. The ignition of hydrogen thermonuclear reactions evidently took place while the central portion of the solar nebula still formed a flattened rotating disk. The nuclear energy released during a possible preceding phase of deuterium burning is too small to modify this conclusion. If we take the D/H ratio in the solar nebula to be 10% of that in the oceans, the density at a given temperature would only be decreased by about 30% during the deuterium-burning process. The dissipation processes leading to the hydrogen ignition should take only a few thousand years[5].

It is a property of a self-gravitating infinite plane distribution of matter that the pressure at the central plane is independent of the temperature[5]. This resembles the situation in an electron-degenerate stellar core. Thus it is possible that the ignition of hydrogen-burning reactions at the centre of the disk can be accompanied by a thermal runaway. This is likely to raise the adiabat of the gas to a higher value than it would attain on the main sequence, expanding the star and forming a body in hydrostatic equilibrium somewhat on the low temperature side of the main sequence in the Hertzsprung-Russell diagram. There would be a rapid rise in the luminosity at this time. This process may explain the sudden flare-up of the star FU Orionis[15].

The process may also account for hitherto puzzling features of the Hertzsprung-Russell diagrams of young clusters. In such clusters the lower luminosity stars are displaced somewhat to the low temperature side of the main sequence. Even the very low luminosity stars are remarkably close to the main sequence; this has seemed to require that they formed many millions of years prior to the higher mass stars[16,17]. But the dissipation times in flat rotating disks having a wide range of masses are probably all comparable to a few thousand years, less than the dispersion in the interstellar collapse times, and the hydrogen flash process then places the resulting stars all quite close to the main sequence.

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Depositional Histories of Sand Grains from Surface Textures

The use of the electron microscope to determine the depositional histories of sand grains is a relatively new but well acclaimed technique[1-6]. The underlying principle is that a detrital quartz grain will bear surface textures that may be related to processes that have operated on it during transportation and deposition.

In 1968 Krinsley and Donahue[4] published micrographs with very full descriptions intended as a glossary of submicrographic sand surface textures. Littoral (beach), aeolian (dune), glacial and diagenetic textures were outlined based on the work of 8 years involving more than 400 sand samples and 4,000 grains. Where possible laboratory duplication of textures was carried out. Krinsley and Donahue stressed the importance that an assemblage of textures should characterize any one abrasive process—a single texture cannot be considered completely diagnostic. An attempt was also made to relate the textures observed to the mechanical or chemical process involved.

I do not intend to undermine the valuable work of Krinsley and Donahue[4], but suggest here some possible reservations in the interpretation of sand grain surface textures.

During the course of an investigation by scanning electron microscope of some Pleistocene sands of controversial origin from NE Cheshire, sand samples were also selected from known environments to act as standards for comparison with the Pleistocene sands. Among these were quartz grains of primary origin from freshly weathered granite in Northumberland and collected from a stream which drained only the granite; beach sands from Studland Heath in Dorset, eroded from Cretaceous Lower Greensand; and freshly weathered Carboniferous Millstone Grit grains from the Goyt River valley, Derbyshire. Carboniferous sandstones are believed to be the principal source rocks of the Pleistocene sands[7]. Because all the standard samples, except the beach sands, were freshly weathered, and the beach sands were collected from an area devoid of glacial deposits, there should have been no indication of glacial abrasion. But the surfaces of very many of these grains frequently show textures closely resembling those described as glacial[4]. Fig. 1 is a micrograph of a primary quartz grain from the Northumberland granite, showing high angularity, high relief and arcuate, semi-parallel fractures. Fig. 2 shows a freshly weathered Millstone Grit grain; the same features are clearly visible. Fig. 3, a micrograph of part of the surface of a quartz grain collected from the beach at Studland Heath, Dorset, shows an arcuate, parallel fracture pattern, with rounding of the fracture probably the result of marine abrasion. A similar feature on a quartz grain from a subantarctic deep sea core has been described by Margolis and Kennett[8] as being produced in a glacial environment and suffering subsequent rounding in an aqueous environment.
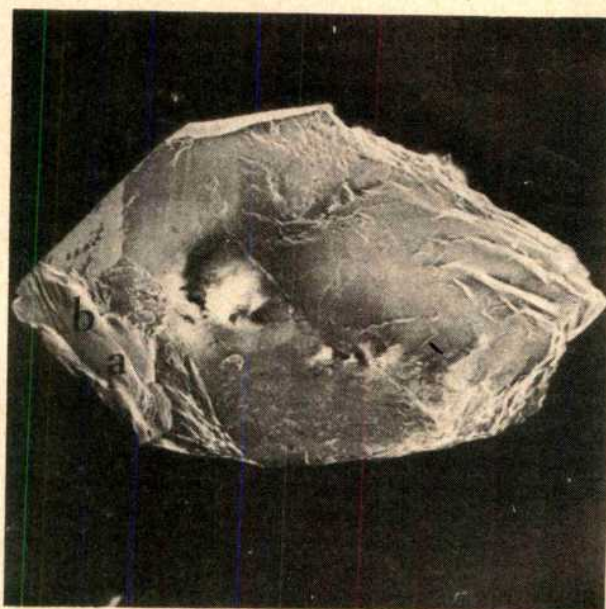
Fig. 1 Micrograph of a quartz grain freshly weathered from Cheviot granite, Northumberland. The grain shows high angularity, fairly high surface relief and both arcuate (a) and parallel (b) fracture patterns. (× 56.)

It thus seems possible that features described as glacial by the earlier criteria[4] may be found on grains from a variety of environments and which have suffered no glaciation.

Krinsley and Margolis[5] stated (with reference to aeolian surface textures): "The meandering pattern results from the intersection of slightly curved conchoidal breakage patterns; the conchoidal pattern is probably caused by grain to grain collision in an aeolian medium. These breakage patterns differ from their glacial counterparts in that they are smaller than the largest glacial breakage pattern and have greater uniformity; they differ from those produced by beach action in that the area enclosed is somewhat rounded and more uniform."

There is no real indication here how to distinguish between small glacial fractures and aeolian fractures. Similarly it is probable that a fracture of any origin will tend to become rounded and the area enclosed uniform if subjected to a period of aqueous abrasion.

Krinsley and Margolis[5] have related the characteristic glacial features of angularity, high relief and large variation in the size of arcuate breakage patterns to the equally large

variety of particle sizes in the glacial environment and the high energy of the transporting medium. It should therefore follow that such features may be produced in any environment where there is a wide variety of particle sizes and high energy conditions. These may include:

Scree slopes where large blocks fall and shatter, and slopes shift periodically to more stable positions. High energy is intermittent and a wide range of particle sizes is produced.

The upper stretches of rivers and streams where there is turbulent flow after heavy rain and a wide particle size range.

The surf zone of a pebble beach where breaking waves pound sand grains onto larger fragments.

In the first two environments the depth of water is shallow and turbulence is sufficient to exceed the protective cushioning effect.

Fig. 2 Micrograph of part of the surface of a quartz grain from freshly weathered Millstone Grit (Goyt Valley, Derbyshire). The micrograph shows several parallel and arcuate fracture patterns. (The apparent rounding of the features is due to incorrect focusing.) (×440.)

The value of any new sedimentological technique lies in its application to the interpretation of ancient deposits where there is no *a priori* knowledge of transporting medium and depositional environment. The origins of the Pleistocene Middle Sands of NE Cheshire have been the subject of some discussion[7,9-12]. Possible processes involved during the transportation and deposition of the sands include fluvial, aeolian, glacial, lacustrine (littoral and deeper water) and solifluction. By use of the Krinsley and Donahue[4] criteria evidence of aqueous, aeolian and glacial abrasion can be distinguished. Fig. 4 is a micrograph of a grain showing fairly typical "glacial" features: high angularity and surface relief, arcuate fractures and surface striations. But this grain was collected from a locality close to the source area of the sands and in a region where glacial drift is evident. Because the transporting medium is believed to have been fluvial[7,12] the textures observed might have resulted from the initial mechanical weathering of the source rocks; transportation in the upper reaches of a periglacial river turbulent with melt-waters; or abrasion during glacial transportation. From this I conclude that if grains are found bearing apparent "glacial" textures, it is possible to say only that these grains have been subjected to a high degree of mechanical abrasion in an environment of high energy where there is a wide range of particle size present.

Although previous work has shown that there is great value

Fig. 3 Micrograph of part of the surface of a quartz grain collected from the beach at Studland Heath, Dorset, and weathered from Cretaceous Lower Greensand. The feature is an arcuate, parallel fracture and rounding is probably the result of marine abrasion. The initial fracture cannot have been produced in a glacial environment. (×920.)

in the study of quartz grain surface textures as an expression of transportational and depositional processes, perhaps more attention should be paid to the dynamics of such processes to determine what combination of physical parameters is required to produce a particular texture and whether such parameters are replicated in different environments. In the case of simple arcuate and parallel fracture patterns and high relief, the physical requirements may be replicated in many environments. Therefore in the study of a known natural, or simulated, environment the conclusion that the assemblage of textures produced in that environment can be used to isolate the environment is false. It is possible to conclude only that these textures may represent that environment but the pos-
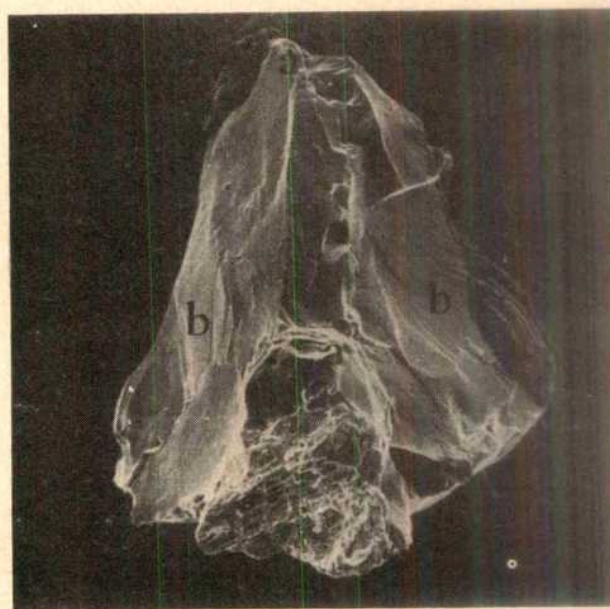
Fig. 4 Micrograph of a quartz grain from Pleistocene Middle Sands of NE Cheshire. This grain is fairly angular, has very high relief and displays many arcuate (a) and parallel (b) fracture patterns. (×88.)

sibility of other environments with similar dynamic properties cannot be eliminated.

I thank British Industrial Sand Ltd for their permission to collect sand samples from NE Cheshire quarries.

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Bubble Models in Two and Three Dimensions

THE bubble raft model described by Simpson and Hodkinson[1] illustrates many of the features of an amorphous alloy. Because the geometrical properties of two and three dimensional space are very different, however, quantitative conclusions drawn from the model must be treated with reserve.

In "crystalline" bubble rafts we see only sections of the one and two dimensional defects (dislocations and grain boundaries respectively), but knowing the lattice repeat in the third dimension we can draw conclusions about the equivalent real crystals. But many properties of the two dimensional model, such as the pair distribution function (PDF), are very different from the three dimensional equivalents, even after maximum correction for obvious geometrical differences.

In a non-crystalline amorphous bubble raft, we know nothing of the molecular arrangements above and below the plane of the model. Moreover, the raft effectively constrains the bubbles to lie in a single plane; this the molecules would not do in reality, but an arbitrary section through the aggregate would intersect most of the molecules within their volumes. Apart from ignoring the third dimension (the characteristics of which are not implied by the two dimensional case) the constraints on the system result in more symmetry in the raft model than in the real aggregate. Thus, conclusions about three dimensional aggregates must be made reservedly unless the particular property is independent of the dimensionality of the aggregate. Dimensionality dependence of properties is implied, for example, by the Ising model (exactly soluble in two dimensions but not in three[2]), and the completely different connectivities of planar square and cubic nets, which give very different random walk characteristics[3] (of relevance to electrical, thermal and mechanical properties).

Structural differences between aggregates can be discussed in terms of a subdivision of the plane (volume) occupied into polygonal (polyhedral) cells by using the Voronoi construction[4,5]. The two dimensional raft (or three dimensional packing) is replaced by r space filling polygons each with N_i edges (r polyhedra with N_i faces). Now in two dimensions

$$\bar{N} = \frac{1}{r}\sum_1^r N_i = 6$$ always, independent of the arrangements of

spheres[6]; in the ordered "crystalline" raft, all polygons are hexagons, while in the disordered "liquid" case, N_i will vary, but $\bar{N}$ will still equal six. The identity of $N_{2D\text{ crystal}}$ and $N_{2D\text{ solid}}$ is demonstrated by the easy "crystallization" of a two dimensional liquid; the liquid phase is continuous with the solid, there is a "liquid"–"crystalline" critical point, no discontinuity at the melting point, and no supercooling. Thus the two dimensional raft contradicts several important liquid properties. In three dimensions, however, $\bar{N}$ changes discontinuously when the crystal melts, reflecting the existence of supercooling, a discontinuous liquid-solid transition, and the lack of a critical point.

With the above in mind, we can now explain the main features of the PDFs in ref. 1, and show how they relate to the real three dimensional case.

The gross features of any PDF at small distances (say < 3 sphere diameters) reflect those local arrangements of spheres which are possible under the external constraints. Thus we can explain the peak positions of the PDF of a hexagonal close-packed (h.c.p.) raft in terms of the equilateral triangles formed in the plane by the component spheres, the peak heights reflecting the frequency of the triangles and other geometrical figures built up from them.

Fig. 1 shows the intermolecular distances found in the PDF up to 4 diameters. Similarly, a three dimensional h.c.p. PDF can be interpreted in terms of tetrahedral and octahedral sphere arrangements, with peaks at intermolecular distances characteristic of those geometrical figures and their multiples.

The polycrystalline PDF (line 2, Table 1) is in part a superposition of the two PDFs of the hexagonal crystalline arrangements of the two components. Although there will be slight shifting in peak positions and smearing of peak profiles (caused by "grain boundaries" and plotting against the mean diameter of the two components), we can interpret the main features of the PDF in terms of the ordered single component hexagonal raft. Thus we have peaks at distances which correspond closely with the common geometrical distances found in the perfect raft.

Table 1 Comparison of Pair Distribution Peak Positions

Peak number	Dimensionality —	1	2	3	4	5	6	7	8	9	10	11	12
(1) Hexagonal crystal raft	2	1.00	1.73	2.0	2.65	3.00		3.46		3.61	4.00 3.85		4.36
(2) Hexagonal polycrystal raft	2	1.00	1.77	2.01	2.65	3.00		3.49		3.61	3.97		4.41
(3) Amorphous raft	2	1.02	1.88	2.04	2.80			3.50		3.73	3.88		4.48
(4) Random close packing	3	1.00	1.73	1.99			2.65		3.47			4.25	
(5) Corresponding vector in Fig. 1	—	1	2	3	4	5	Complex 6 (see text)	Complex 7		8		Complex 9	
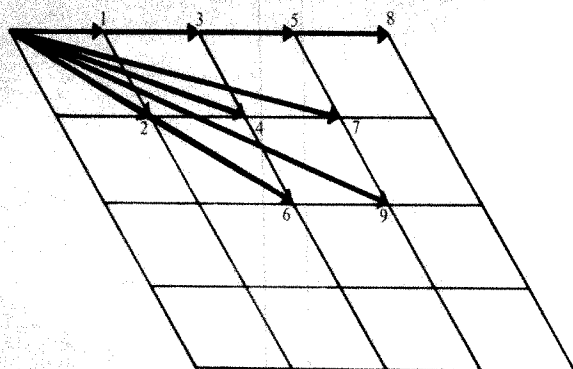
Fig. 1 Vectors of length less than 4.5 sphere diameters in a planar hexagonal lattice. The numbers correspond to those in Table 1 of ref. 1, and also to those in the bottom line of my Table 1.

Partly because the dimensions of the basic geometrical units will vary more (and small proportions of, for example, squares will arise) we expect more PDF blurring for the amorphous bubble raft (line 3, Table 1); we can, however, still interpret the low order peaks in terms of the perfect hexagonal raft (again reflecting the continuity of the two dimensional crystal and amorphous arrays). The peak positions are displaced somewhat from the "crystal" positions, and the peak at 2.80 is the result of a "smearing" together of the "crystal" 2.65 and 3.00 peaks, but in all three cases above, these low order peaks are produced by the same local geometrical arrangements of spheres: equilateral (crystal) and distorted (amorphous) triangles.

Now consider the PDF of the three dimensional random packing (RCP) of equal spheres. The peak positions are plotted on line 4, Table 1, so that only peaks arising from the same geometrical arrangement of neighbours are placed in the same column. Peaks 1, 2 and 3 correspond to peaks in the previous three PDFs because they arise from the same two dimensional arrangements of spheres which of necessity must be present even in an RCP (again, see Fig. 1). Peak 6, however, does not arise from the same source as peak 4, but comes from averaging over several distances between 2.45 and 2.90 in non-crystalline aggregates of tetrahedra (Bernal's pseudonuclei[7]); hence its structural significance is totally different from that of peak 4. From peak 6 outwards the RCP function bears little resemblance to the two dimensional PDFs: peaks 5, 9 and 10 are missing (and an absent peak is significant structurally), and peak 8 arises from complex arrangements very different from peak 7. Thus, even ignoring peak heights and profiles, the RCP bears little significant structural resemblance to the two dimensional packings, the coincidence at low distances being due to the necessary existence in a three dimensional packing of two dimensional arrangements of 2, 3 and 4 closely-spaced spheres. Looking at peak heights and profiles, we find an even greater divergence, reflecting the greater variability of local arrangements in the RCP case.

By examining the relevant geometrical ideas, we can also begin to understand the data of ref. 1 drawn from the rafts concerning solubility and Végard's law (we consider interstice sizes and variability), collineations (local sphere arrangements) and mechanical properties (out of plane movements of spheres); these again cause us to beware of extrapolating too much into three dimensions from two.

In summary, while wholeheartedly subscribing to the illustrative and qualitative values of two-dimensional models, we must not over-extrapolate into three dimensions, where the geometrical properties of space are different. Comparing two and three-dimensional models and packings is not only difficult but is of limited value. As a model of a very thin amorphous alloy (a few molecular diameters thick), however, the bubble raft model could have great specific predictive value.

Moreover, a close examination of the behaviour of a two-dimensional PDF when composition and/or radius ratio of the components are varied would be interesting in itself.

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BIOLOGICAL SCIENCES

Stimulation of Division of Density Inhibited Fibroblasts by Glucocorticoids

THE division of most "normal" cells in culture is inhibited after they have grown to a confluent monolayer. This is not the case with cells transformed either spontaneously or by tumour viruses[1]. Alterations of the surface membrane might be partly responsible for this uncontrolled growth[2]: for example, protease action at the surface of contact-inhibited cells causes them to divide[3,4] and acquire surface properties characteristic of malignant cells, such as increased agglutinability by plant lectins[5,6]. Neuraminidase[7] and hyaluronidase[8] can also initiate division of contact-inhibited cells. Transformed cells contain abnormally large concentrations of proteases and glycosidases[9,10] which are presumed to be lysosomal enzymes. Since cortisol stabilizes lysosomal membranes[11], we decided to investigate its effect on the growth of cells not subject to density inhibition of division: we found very little effect on 3T6, L, polyoma-transformed 3T3 (Py3T3) and SV40-transformed 3T3 (SV3T3) cells. However, cortisol unexpectedly stimulated DNA synthesis and division of density-inhibited 3T3 cells. This stimulation was specific for cells subject to contact inhibition of division. Density-inhibited early passage diploid human foreskin fibroblasts (HF cells) were similarly stimulated by cortisol. In addition, the stimulation was specific for steroids with high levels of glucocorticoid activity. The stimulation appears to involve changes in the cell surface, for treated 3T3 cells were agglutinated to a greater degree by concanavalin A than control cells.

Cells were grown as previously described[12] in Dulbecco-Vogt modified Eagle's medium containing 10% calf serum (3T3, Py3T3, and SV3T3 cells), 10% foetal calf serum (L cells), or 1.5–3% calf serum (HF cells, given by Dr David T. Kingsbury). We found no evidence of mycoplasma contamination of any cells following autoradiography with ³H-thymidine[13]. Neither control nor treated cells took up trypan blue or eosin Y dye, indicating that stimulation was not due to local areas of cell death. Agglutination by concanavalin A was determined as described before[14].

The stimulation of DNA synthesis by confluent 3T3 cells showed a typical dose-response relationship (Fig. 1). The rate of synthesis was measured 23 h after addition of cortisol, the time of maximal stimulation. Addition of cortisol to final
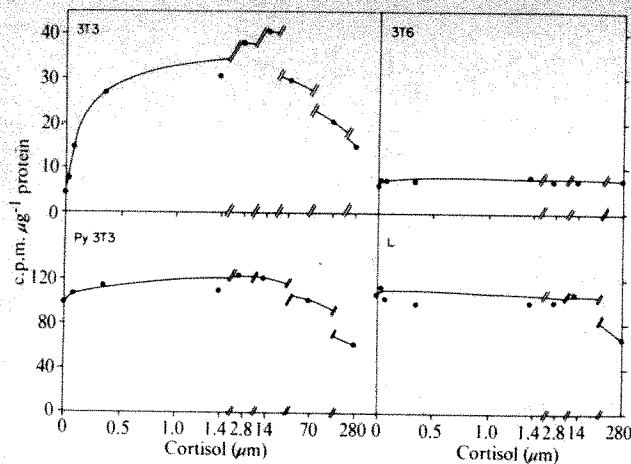
Fig. 1 Effect of cortisol on DNA synthesis by confluent 3T3, 3T6, Py3T3 and L cells. 1.5×10^5 cells were plated per 35 mm Falcon plastic tissue culture dish in 2 ml. of medium. After growth to confluency, cortisol (in ethanol) was added to the final designated concentration. The final ethanol concentration was usually 0.5% and never exceeded 1%, concentrations which had no effect on DNA synthesis or cell division. The cells were labelled for 15 min with ^{3}H-thymidine (2.5 µCi/ml.; 0.4 Ci/mmol) 23 h after adding cortisol. They were then washed twice with cold phosphate-buffered saline, five times with cold 10% TCA, dissolved in 0.5 M KOH, and neutralized with HCl. Radioactivity was measured by liquid scintillation. Each point represents at least four determinations.

levels of 3.4×10^{-7} M to 2.8×10^{-5} M caused a six to nine-fold increase in the rate of thymidine incorporation into DNA. (The normal serum concentration of cortisol is about 3×10^{-7} M[15], a concentration which produced a five-fold stimulation of thymidine incorporation.) Addition of 5×10^{-6} M cortisol to growing non-confluent 3T3 cells increased the rate of DNA synthesis only two-fold, even though it increased the final saturation density by 60%.

Stimulation was specific for contact-inhibited cells. As Fig. 1 shows, confluent cultures of Py3T3, 3T6 and L cells (from a C3H fibrosarcoma) responded only slightly to levels of cortisol which greatly stimulated 3T3 and HF cells. In addition, there was no significant stimulation or inhibition of DNA synthesis in non-confluent L and Py3T3 cells following cortisol treatment. The specificity was not simply a consequence of the very slow growth of confluent 3T3 and HF cells; slowly growing SV3T3 cells (in medium containing 0.15% serum) were as unresponsive as were growing SV3T3 cells.
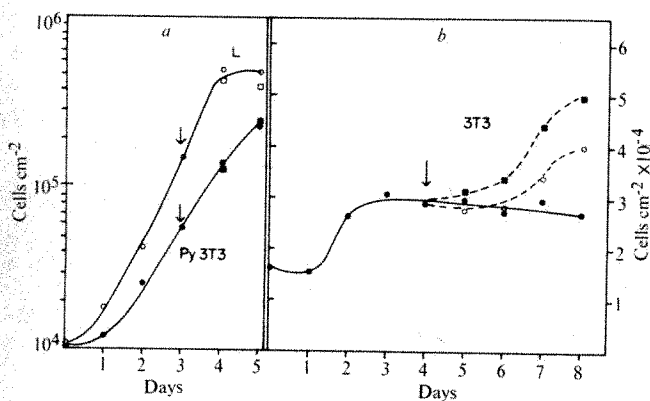
Fig. 2 Effect of cortisol on 3T3, Py3T3 and L cell number. Cells were plated at the indicated densities in 35 mm dishes. Cortisol was added to confluent cells at the times indicated by arrows. Cells were suspended with trypsin and counted in a haemocytometer. a: ○, L cells; □, L cells+14 µM cortisol; ●, Py cells; ■, Py cells+14 µM cortisol. b: ●, 3T3 cells; ○, 3T3 cells+0.07 µM cortisol; ■, 3T3 cells+14 µM cortisol. Each point represents quadruplicate counts on duplicate plates.

Cortisol markedly stimulated division of contact-inhibited fibroblasts. Addition of cortisol to confluent 3T3 cells to 1.4×10^{-5} M produced an 85% increase in cell number (Fig. 2). The stimulatory action on contact-inhibited cells was confirmed with confluent cultures of the early passage human diploid fibroblasts; 2.8×10^{-5} M cortisol in the same conditions produced a 41% increase in cell number. Inclusion of 1×10^{-5} M N^6,O$^{2'}$-dibutyryl cyclic AMP (dibutyryl cyclic AMP) with the cortisol did not reduce the stimulatory effect on confluent 3T3 cells. This same concentration of dibutyryl cyclic AMP suppresses almost totally the stimulation of cell division brought about by trypsin[16]. A higher concentration of dibutyryl cyclic AMP (1×10^{-3} M) partially reversed the cortisol stimulation of DNA synthesis and cell division.

The morphology of the 3T3 cells 4 days after addition of cortisol resembled that of transformed cells. They seemed to be layered on top of each other, and cell processes overlapped.

In contrast to the stimulation of division of contact-inhibited cells, no significant increase in cell number was detected when confluent L or Py3T3 cells were treated with cortisol (Fig. 2).
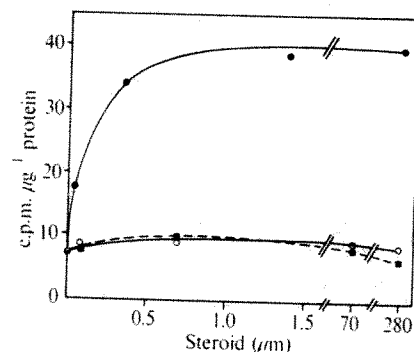
Fig. 3 Effect of cortisol, progesterone and cholesterol on DNA synthesis by confluent 3T3 cells. Culture and assay conditions were identical to those for 3T3 cells given in Fig. 1. (Each point is the average of duplicate determinations.) ●, Cortisol; ○, cholesterol; ■, progesterone.

The stimulatory effect was specific not only to cell type but also to steroid. As Fig. 3 shows, broad concentrations of cholesterol and progesterone had virtually no effect on the rate of DNA synthesis 23 h after addition to confluent 3T3 cells. To rule out the possibility that a peak of DNA synthesis occurred at a time different from 23 h, we measured rates at 8 h intervals from 0–48 h. Neither cholesterol nor progesterone produced increases in thymidine incorporation at these times. In addition, no significant increase in cell number was detected by 60 h after addition of 1×10^{-4} M cholesterol or 2×10^{-5} M progesterone. The synthetic glucocorticoid, triamcinolone acetonide, added at 2.5×10^{-7} M, caused a 3.5-fold stimulation of DNA synthesis in confluent 3T3 cells 23 h after addition.

Agglutination of confluent 3T3 cells by 250 µg/ml. concanavalin A was markedly increased over controls after 1 h of treatment with 1.4×10^{-6} M cortisol, suggesting not only that DNA synthesis and cell division might be initiated by a relatively brief treatment with cortisol, but also that the stimulatory action of cortisol might result from changes it elicits in the surface membrane. Induction of tyrosine amino-transferase in hepatoma cells by cortisol correlates with altered surface properties[17], and increased agglutination by wheat germ lipase agglutinin has been demonstrated after glucocorticoid treatment of HeLa cells[18].

Cortisol has diverse effects on mammalian cells: it is cytotoxic to lymphoid cells[19], inhibits DNA synthesis and division of L929 cells[20], and leads to the induction in hepatic and hepatoma cells of enzymes involved in amino-acid catabolism[17,21]. Specific cytoplasmic glucocorticoid receptors have been demonstrated in lymphoma[22], L929[23] and hepatoma[24] cells. Glucocorticoid-resistant cell lines have been

derived from the lymphoma[22] and L929[23] cell lines, and the resistance seems to be due to decreased cytoplasmic glucocorticoid binding capability. We are investigating the possibility that transformation of 3T3 cells by tumour viruses decreases the glucocorticoid binding capability of the cells.

Several observations suggest that cortisol stimulates division of contact-inhibited cells by altering acid mucopolysaccharide metabolism. (a) Cortisol inhibits the synthesis of acid mucopolysaccharides in skin and connective tissue[25]. (b) The intrinsic viscosity of hyaluronic acid secreted by human synovial cells is reduced by cortisol treatment and during rapid cell growth[26]. (c) Treatment of density-inhibited secondary mouse embryo cells with hyaluronidase causes cell division[8]. (d) Transformation of 3T3 cells by polyoma or SV40 viruses causes decreased synthesis of hyaluronic acid[27]. This system should lend itself to biochemical analysis to test the above as well as alternative mechanisms.

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Preliminary Evidence for Cholinoceptive Sites in the Excitability of Spermatozoa

THE spermatozoa of a variety of species respond to mechanical stimuli and to other physical and chemical alterations in the environment by changing speed and pattern of movement,
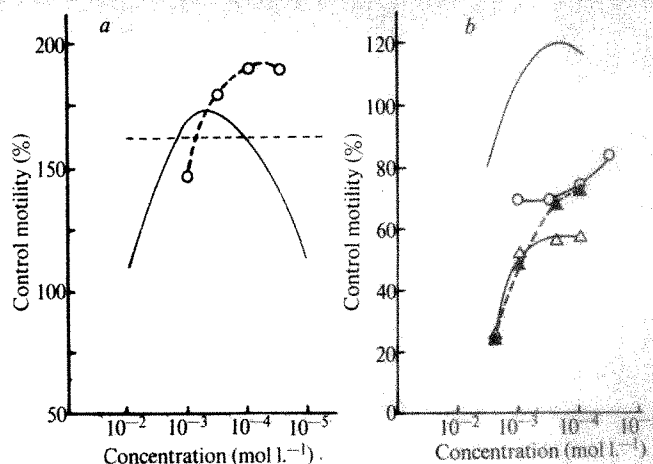
Fig. 1 Sea urchin sperm motility. a, Sperm cells suspended in filtered seawater containing 20 mM dimethyl sulphoxide. Solid line without data points, redrawn from ref. 2. Open circles, effect of adding varying concentrations of d-tubocurarine (curare) to sperm suspension containing 100 µM acetylcholine. Dashed line indicates swimming rate of sea urchin sperm in 100 µM acetylcholine and DMSO without curare. b, Sperm cells suspended in filtered seawater containing 20 mM dimethyl sulphoxide (except for solid line without data points, redrawn from ref. 2, in which no DMSO was present). Open circles, effect of varying concentrations of curare on sperm swimming speed in filtered seawater containing 20 mM DMSO. Open triangles, effect of adding varying amounts of acetylcholine to sperm exposed to 100 µM curare; and closed triangles, sperm exposed to 1 mM curare before adding acetylcholine.

amplitude, frequency and length of the flagellar wave, as well as membrane potential[1-4]. The propagation of the flagellar wave thus cannot be attributed entirely to an autonomous oscillator, but must be influenced in a "neurochemical" fashion analogous to smooth muscle control systems.

Spermatozoa from mammals, fishes, echinoderms and molluscs possess highly active cholinesterases[5]; the swimming speed of mussel, sea urchin and starfish sperm cells changes biphasically and in dose-dependent fashion in eserine and diisopropylfluorophosphate as well as in acetylcholine and curare[1,2]. Motility is conveniently measured by the centrifuge-orientation, absorbance change method[2]. Acetylcholine and curare[1,2] both increase and decrease the velocity of sea urchin sperm by about 20% or less depending on the concentration. Dimethyl sulphoxide, which at a concentration of 20 mmol l.[-1] does not visibly affect sperm motility but facilitates permeation by the pharmacological agents, permits 1 mM acetylcholine to cause an initial increase in sperm movement to 170% of the control rate[2]. Curare, when added with DMSO, causes a 25-30% reduction in motility in the same concentration range that maximally increased the swim rate[2] in the absence of DMSO (Fig. 1a and b).

Examination of the effects of the interaction of these two drugs reveals that, in DMSO, 1 mM acetylcholine (which optimally increased the sperm cell velocity) now, in combination with curare, doubles the inhibitory effect of the curare alone (Fig. 1b). Raising the acetylcholine concentration to 4 mmol l.[-1], while holding the curare at 100 µM, further depresses the swimming speed to 25% of the control rate. Acetylcholine in equimolar concentrations with the curare (100 µmol l.[-1]) acts neither synergistically nor antagonistically on the curarized spermatozoa. On the other hand, addition of curare to sperm cells pretreated with 100 µM acetylcholine again results in a biphasic, dose-dependent response (Fig. 1a). Curare in ten-fold excess of the acetylcholine (curare/ACh=1 mmol/100 µmol) reduces the sperm speed to 150% of the control from the 165% without curare, while at a 5 to 1 ratio the swim rate goes up to 180% of the control. With both at equimolar concentrations and at a 1 to 2 ratio (curare/ACh=50 µmol/100 µmol) the swim speed now increases to 190% of the control

rate. The order of the drug administration is apparently quite consequential.

Decamethonium, another pharmacologic agent which reportedly acts on the receptor sites at synapses and neuro-muscular junctions in vertebrates, also affects the motility of sea urchin sperm cells. Concentrations of decamethonium in seawater above 10 μM depress the swimming speed, while at 10 μM or below there is a slight increase above the control swim rate. In the vertebrate system depolarization induced by decamethonium appears initially to stimulate then block impulse transmission[6]. The sperm cells' response may be regarded as comparable; presumably irreversible depolarization occurring more rapidly at the higher concentrations and re-quiring longer exposure at the lower concentrations, the stimulatory effect of the low concentration of decamethonium persists long enough to be detected by my method.
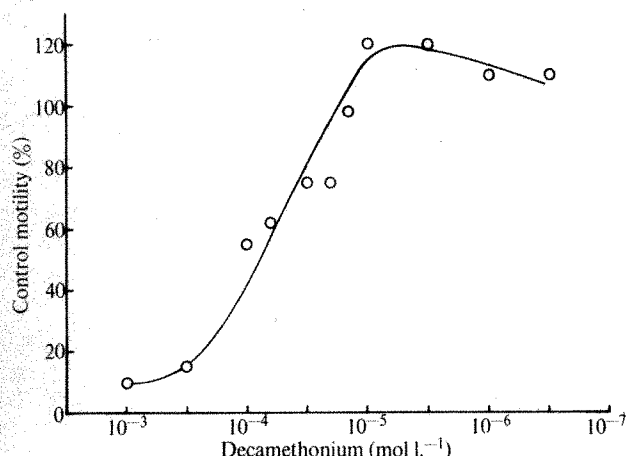
Fig. 2 Sperm cells suspended in filtered seawater. Effects of varying concentrations of decamethonium.

These preliminary observations appear to lend support to the thesis that an intracellular control system, cholinergic in nature, imposes a modulatory effect on the purely contractile components which underlie flagellar wave propagation[2]. Moreover, this cellular "governor", under appropriate circum-stances, may serve to mediate the effects of some extraneous factors on sperm motility. If decamethonium's primary pharma-cologic action does indeed depend on its depolarization effects, the data presented here are further consistent with our interpre-tation that changes in the membrane potential bear a causal relationship to the sperm cell's motile performance[3]. Dryl's description[7] of the role of the cell membrane of ciliates in both the reception of external stimuli and in stimulus conduction may have some bearing relative to the nature of spermatozoan response mechanisms.

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Headspace Volatiles of Marijuana

THE sweet odour of Cannabis sativa, L. is of special interest as a possible means for the detection of illicit marijuana traffic. US Customs dogs, trained to alert to the odour of marijuana and hashish, are successfully used to find concealed contraband. An electronic "sniffer" that employs a portable quadrupole mass spectrometer to detect volatile vapours of drugs, including marijuana, has also been demonstrated[1]. Although the chemical composition of the essential oil of marijuana has been thoroughly investigated[2-4], little is known about the specific composition of the emitted aroma constituents. The composition of this headspace, as it contributes directly to the odour, is more significant than that of the oil for the charac-terization of marijuana aroma[5]. Aroma profiles of fruits and vegetables have been obtained by direct gas chromatographic analysis of the headspace components[6]. We used this tech-nique, which permits rapid determination of labile constituents under mild analytical conditions, to analyse marijuana aroma, and we report our preliminary results here.

An authentic marijuana standard containing 1.9% Δ^9-THC and grown from Mexican seed was obtained (National Insti-tute of Mental Health programme, University of Mississippi School of Pharmacy). Additional samples of marijuana ranging in Δ^9-THC content from 1.4% to 3.1% were obtained from Customs' seizures. All samples were stored at $-25°$ C. Authentic samples of mono- and sesqui-terpenes and other compounds detected in the headspace were obtained from commercial sources or donated.

Marijuana was prepared routinely for vapour sampling by placing 1 g in a microvial fitted with an on-off valve and septum, and after equilibration for 1 h at 65° C, 5 ml. of the headspace air containing the volatiles was withdrawn using a gastight syringe and immediately injected into a gas chroma-tograph. The aroma profiles obtained included compounds present in the headspace at concentrations as low as 0.1 ng ml.$^{-1}$, which is below the human odour threshold for many odorants[7]. A 'Perkin-Elmer 900' and a 'Hewlett Packard 7610A' chroma-tograph, equipped with flame ionization detectors and inter-faced with a 'Perkin-Elmer PEP-1' gas chromatography data system, were used. Chromatography was carried out using six-foot glass columns (2 mm i.d.) packed with 3% 'OV-101' on 100/120 'Gas Chrom Q' or 20% 'Reoplex 400' on 80/100 'Chromosorb W', acid washed, with helium as carrier gas (50 ml. min^{-1}). The columns were programmed from 35° C ('OV-101') or 60° C ('Reoplex 400') to 130° C at 6° C min^{-1} to obtain complete headspace chromatograms. A third column packed with 'Chromosorb 101', 80/100 was operated at 90° C to separate certain of the low-boiling components.

Typical headspace chromatograms show three separate frac-tions based on ascending order of component boiling points: Fraction I consists of oxygenated compounds (MW < 100); Fraction II consists of mono-terpene hydrocarbons and oxygenated compounds (MW > 100); Fraction III consists of sesqui-terpene hydrocarbons (MW > 200). Separated con-stituents were identified by comparison of their relative retention times (RRT) obtained on the adsorption columns of different polarity with the RRT of authentic standards, and by their mass spectra obtained in separate experiments using a 'Finnigan 3000 GC-MS' system with computer data acquisi-tion. Examination of Fraction I using the 'Chromosorb 101' column confirmed the presence of acetone (approximately 75% of this fraction) and smaller amounts of methanol, acetaldehyde, ethanol, methyl acetate and iso-butyraldehyde. As these com-pounds are commonly found in most plant vapours and are not unique, Fraction I, comprising approximately 10% of the total headspace, was not analysed further.

The components found in Fractions II and III and their RRT as separated on the two columns are listed in Table 1. It is of interest to note that 2-methyl-2-heptene-6-one has not been previously reported as a constituent of marijuana. The relative percentage composition of the headspace components

Table 1 Relative Retention Times of Components of Marijuana Headspace

Component	3% OV 101 32° C (ref. limonene)	3% OV 101 90° C (ref. β caryo-phyllene)	20% Reo-plex 80° C (ref. limonene)	20% Reo-plex 120° C (ref. β caryo-phyllene)
α-Pinene	0.46		0.37	
Camphene	0.51		0.49	
β-Pinene	0.63		0.60	
2-Methyl-2-heptene-6-one	0.62			0.32
Myrcene	0.77		0.78	
Δ³-Carene	0.86		0.69	
α-Terpinene	0.90		0.89	
Limonene	1.00		1.00	
β-Phellandrene	1.00		1.07	
cis-Ocimene	1.14		1.19	
trans-Ocimene	1.24		1.32	
γ-Terpinene	1.28		1.29	
Terpinolene	1.63		1.59	
Linalool	1.84			0.73
β-Caryophyllene		1.00		1.00
trans-α-Bergamotene		1.12		0.87
β-Farnesene		1.26		1.23
Humulene		1.19		1.39

was determined by integration of the area under each peak appearing in the chromatograms (Fractions II and III only), and a typical analysis is shown in Table 2. Data showing the composition of the oil of marijuana obtained by analysis of a steam distillate of the standard sample are included for comparison. Fenchyl alcohol, borneol, β-bisabolene and 2-methyl-2-heptene-6-one are components not previously reported in the oil[4]. As indicated in Table 2, quantitative results accounted for 98.3% of the headspace components of Fractions II and III and 96% of the oil. The remaining 1.7% of the headspace consists of one unidentified mono-terpene hydrocarbon; the remaining 4% of the oil is composed of unidentified mono-terpene alcohols (1%) and sesqui-terpene alcohols (3%).

Numerous seizure samples of Mexican marijuana were examined and similar headspace profiles were obtained. It is apparent from the data recorded in Table 2 that the com-

Table 2 Comparison of Headspace Composition of Marijuana with Composition of Essential Oil

Component	Composition (%) Headspace	Composition (%) Essential oil
α-Pinene	55.5	3.9
Camphene	0.9	0.7
β-Pinene	16.4	2.2
2-Methyl-2-heptene-6-one *	0.4	0.6
Δ³-Carene	0.6	0.1
Myrcene	8.3	1.0
α-Terpinene	t †	t
Limonene β-Phellandrene	5.4	1.0
cis-Ocimene	1.2	0.2
trans-Ocimene	3.2	0.7
γ-Terpinene	t	t
Terpinolene	0.8	0.6
p-Cymene	—	0.1
Linalool	t	0.5
Fenchyl alcohol *	—	0.1
Borneol *	—	t
trans-α-Bergamotene	0.7	8.0
β-Caryophyllene	3.4	37.5
β-Farnesene	0.8	9.8
α-Terpinenol	—	1.0
β-Humulene	0.7	13.9
α-Selinene	—	2.2
β-Bisabolene *	—	3.2
Curcumene	—	1.4
Caryophyllene oxide	—	7.4
Total identified components	98.3	96.0

* Not previously reported as constituent of marijuana.
† t, trace, <0.1%.

position of the headspace differs markedly from that of the oil, as fewer components are present in different relative proportions. The principal constituents comprising about 85% of the headspace (α-pinene, β-pinene, myrcene, limonene) represent less than 10% of the oil. The minor contribution of oxygenated terpenes to the headspace is shown by the fact that fenchyl alcohol, borneol, and α-terpinenol are all present in the oil but none was detected in the headspace. These results can be explained largely on the basis of the lower volatility of the alcohols. The greater affinity of the oxygenated species for the plant medium, however, vis à vis the terpene hydrocarbons is also a significant factor. The compound p-cymene found in the oil but not in the headspace may be an artefact formed during preparation of the oil[8].

The present unique analysis of the headspace composition is of fundamental value in the characterization of the aroma of marijuana as it reflects the relative volatility of the plant constituents and the complex manner through which these constituents are bound in the plant. The examination of the headspace of marijuana samples of different geographic origin is under study. These data will thus provide the basis for an investigation of the complex biochemical mechanism involved in the detection of marijuana by detector dogs.

We thank V. Venturella for help in examination of Fraction I, C. Erikson for preparation of the oil of marijuana and Givaudan Corp., Clifton, NJ., Fritsche D and O, Inc., New York, and Hercules, Inc., Wilmington, Delaware, for providing samples of headspace compounds.

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Effects of Marijuana and Tobacco Smoke on DNA and Chromosomal Complement in Human Lung Explants

HUMAN lung explants exposed to smoke from marijuana or from Kentucky Standard tobacco cigarettes have been reported to display abnormalities of cell morphology, mitosis, DNA synthesis and atypical proliferation[1]. We report here a study designed to test the effects of both types of smoke on the DNA and chromosomal complement.

We used the model system for exposing lung explants to puffs of fresh smoke in standardized conditions[2]. Lung explants were prepared and exposed to cigarettes made from marijuana or Kentucky Standard tobacco as previously described[1]. Normal lung tissue was obtained not only from older patients operated on for pulmonary tumours[1], but also from a healthy young man (age 25 yr) killed in an accident. The DNA determinations were carried out in metaphases and telophases of the original stained lung cultures by Feulgen microfluorometry[2]. All together, over 2,000 cells were examined in control cultures and correspond-

ing cultures from 4–70 days after exposure to marijuana or tobacco cigarette smoke. Chromosomes were prepared according to Inui et al.[3] for the examination of chromosomal status.

Results were reproducible in all cultures. They were essentially the same for cultures derived from the lungs of the older tumour patients and from those derived from the healthy young man. There was a good agreement between chromosomal and DNA data.

Table 1 Comparison between the DNA Content* in Metaphases and Telophases†, and Number of Chromosomes‡ in Fibroblastic Cells of a Control Adult Human Lung Explant and after Exposure to Fresh Smoke from Marijuana and Kentucky Standard Cigarettes

Type of experiment	Mean frequency in per cent					
	DNA content in metaphases		DNA content in telophases		Number of chromosomes	
	4 DNA	≷ 4 DNA	2 DNA	≷ 2 DNA	2 N	≷ 2 N
Control	76	24	70	30	56	44
Kentucky Standard	56 pCo=0.01	44	48 pCo<0.0065	52	36 pCo<0.0005	64
Marijuana	52 pCo=0.0025	48	52 pCo<0.005	48	31 pCo<0.0005	69

* Microfluorometry.
† 431 cells measured.
‡ 633 metaphases counted.

There were significant differences between control and exposed cultures; 4–28 days after exposure to marijuana or Kentucky tobacco cigarettes there was not only a significant decrease in number of cells with 2 N, and with 4 DNA and 2 DNA (Table 1), but the variability of cells with deviating DNA content and chromosomal numbers was greater than that observed in controls (Figs. 1 and 2). This difference was especially marked after marijuana cigarette smoke.

It thus seems that exposure of human lung explants to fresh smoke from marijuana or Kentucky Standard tobacco cigarettes evokes not only abnormalities in DNA synthesis, mitosis and growth[1], but also results in alterations of DNA and chromosomal complement, that is in a disturbance of the genetic equilibrium of the cell population. The finding that these changes were

Fig. 2 Comparison between the number of chromosomes of fibroblastic cells (number of metaphases counted = 633) from (a) control adult human lung explant and after exposure to fresh smoke from (c) marijuana and (b) Kentucky Standard cigarettes (number of cultures examined = 12).

observed very early, and that they persisted for prolonged periods after exposure, indicates that these alterations are not lethal to the cells. The question whether the cells with abnormal DNA and chromosomal complement are responsible for the subsequent atypical growth, and may represent an early stage preceding malignant transformation, cannot be answered at present.

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Fig. 1 Comparison between the DNA content (Feulgen microfluorometry) in metaphases (M) and telophases (T) of fibroblastic cells (number measured = 431) from (a) control adult human lung explant, and after exposure to fresh smoke from (c) marijuana, and (b) Kentucky Standard cigarettes (5 experiments).

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Specific Biosynthesis of an Envelope Protein of *Escherichia coli*

A UNIQUE structural protein in the envelope of *Escherichia coli*, of molecular weight about 7,500 and covalently attached to the peptidoglycan, was found by Braun *et al.*[1-4], who reported that its amino-acid sequence lacks histidine, proline, glycine, cysteine, phenylalanine and tryptophan[4]. Recently we found that this lipoprotein exists in the *E. coli* envelope fraction not only in the bound form found by Braun *et al.*[1-3] but also in a free form, not covalently attached to the peptidoglycan[5]. This form accounts for about two-thirds of the lipoprotein and serves as a precursor of the bound form[5]. We describe here an *in vivo* situation in which only this lipoprotein is biosynthesized. Using these conditions, we have investigated the biosynthetic mechanism of this envelope protein.
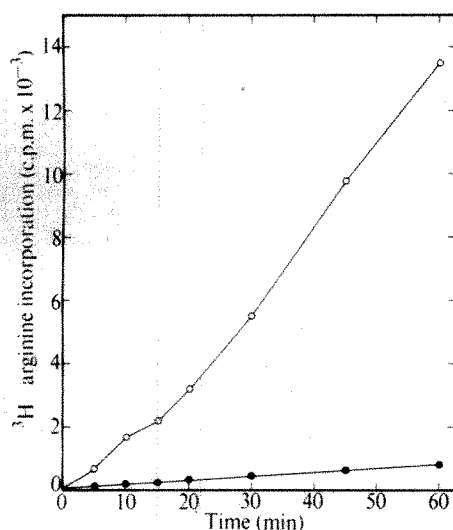
Fig. 1 ^{3}H-arginine incorporation into hot TCA-insoluble fraction in the presence or absence of histidine. *E. coli* CP78 (RC+his−leu−thr−arg−B$_1$−)[6] was grown at 41° C in M9 medium containing all necessary supplements (20 μg/ml. of each amino-acid and 2 μg/ml. of thiamine). At about 2×10^8 cells/ml., 20 ml. of the culture was filtered with an HA 'Millipore' filter and washed with M9 medium lacking histidine. Then the cells were resuspended in 20 ml. of M9 medium containing all necessary supplements except histidine. To 1 ml. of the suspension was added 2 μCi of ^{3}H-arginine (without histidine) and to another 1 ml. of the suspended cells 2 μCi of ^{3}H-arginine and 20 μg of histidine (+histidine). They were then incubated at 41° C. At the time intervals indicated in the figure, 0.1 ml. of the cell suspension was applied to a filter paper disk (Whatman 3 MM, 2.4 cm diameter). Immediately after the sample was spread throughout the disk, it was put into chilled 5% TCA solution containing 100 μg/ml. unlabelled arginine and kept standing in the ice bath for 60 min. These disks were then boiled for 30 min in a 5% TCA solution. After cooling, they were washed three times by changing the TCA solution, soaked in acetone, and dried. Radioactivity was determined in a liquid scintillation counter. ○, With histidine; ●, without histidine.

We have investigated whether this lipoprotein is biosynthesized in cells starved for one of the amino-acids which it lacks[4]. We measured ^{3}H-arginine incorporation into the hot trichloroacetic acid (TCA) insoluble fraction in the presence and absence of histidine using a histidine auxotroph, *E. coli* CP78[6](RC+his−leu−thr−arg−B$_1$−; given by Dr J. Gallant). As Fig. 1 shows, about 95% of total incorporation was inhibited by histidine starvation. Although the rate of incorporation was strikingly reduced in the absence of histidine, ^{3}H-arginine continued to be incorporated into the protein fraction at a low but constant rate. This suggests that some proteins lacking histidine, such as the lipoprotein described here, are produced preferentially during the histidine starvation. We
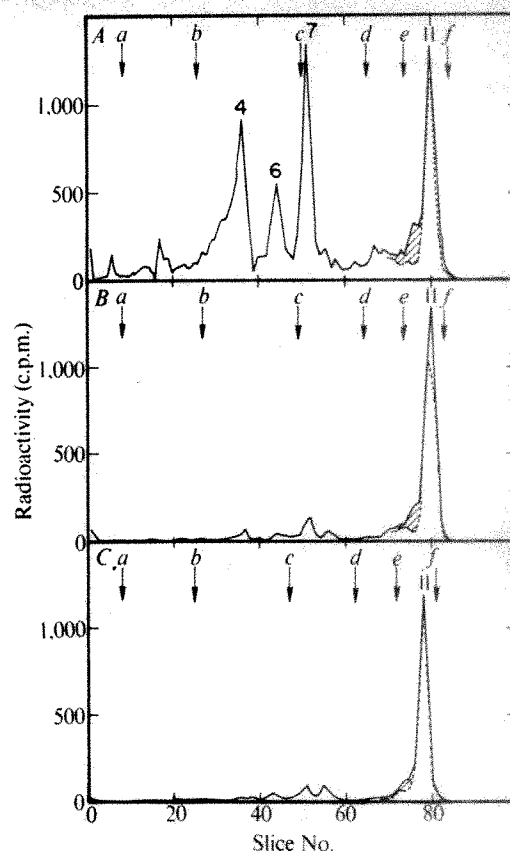
Fig. 2 SDS polyacrylamide gel electrophoresis of the envelope fractions labelled with ^{14}C-arginine in the presence and absence of histidine. Fifty ml. of an exponential culture (about 4×10^8 cells/ml.) of *E. coli* CP78 was filtered and the cells were resuspended in 50 ml. of M9 medium lacking histidine. *A*, Control: 10 ml. of the suspension was diluted twice with M9 medium. ^{14}C-arginine (5 μCi) and 20 μg/ml. histidine (final concentration) was added to the culture, and it was incubated for 1 h at 41° C. The turbidity increased from 53 to 106 Klett units during incubation. *B*, Without histidine (0~1 h): to 20 ml. of the suspension was added 5 μCi of ^{14}C-arginine and the mixture was incubated for 1 h at 41° C. The turbidity increased from 106 to 111 Klett units during the incubation. *C*, Without histidine (2–4 h): 20 ml. of the suspension was incubated for 2 h at 41° C. The 5 μCi of ^{14}C-arginine was added to the culture and it was incubated for another 2 h. The turbidity increased from 106 to 118 Klett units during the whole incubation period (4 h). Envelope fractions were prepared by differential centrifugation as previously described[7]. Half of each envelope fraction was treated with T4 phage lysozyme to analyse the bound form of the lipoprotein as described previously[5]. Both fractions (T4 phage lysozyme treated and untreated) were then solubilized and subjected to SDS gel electrophoresis (7.5% acrylamide gels) in separate gels. Gel electrophoresis was carried out with DANS-internal standards of molecular weights[8]. The patterns of the envelope fractions with and without the lysozyme treatment were superimposed with the aid of the internal standards. ——, Envelope fractions treated with T4 phage lysozyme; - - - -, without T4 phage treatment. In the case of the fraction without the treatment, only the part between *e* and *f* is shown. Positions of internal standards of molecular weight are shown by small arrows; *a*, dimer; *b*, monomer of DANS-bovine serum albumin; *c*, dimer; *d*, monomer of DANS-hen egg white lysozyme; *e*, cytochrome c; *f*, DANS-insulin. Peak numbers correspond to those previously reported[7].

therefore analysed envelope proteins synthesized in the presence of ^{14}C-arginine but in the absence of histidine by sodium dodecyl sulphate gel electrophoresis. As Fig. 2*B* and *C* show, ^{14}C-arginine was almost exclusively incorporated into peak 11 in the absence of histidine, in contrast to the situation in the presence of histidine (Fig. 2*A*). There was substantial incorporation of ^{14}C-arginine into peak 11 not only during the first hour but also between 2 and 4 h after removal of histidine (Fig. 2*B* and *C*).

We have shown previously that the free form of the lipoprotein forms peak 11 and the bound form gives rise to a

shoulder at the higher molecular weight side of peak 11 after lysozyme treatment of the envelope fraction[5]. Fig. 2 also shows the analysis of the bound form (shaded in Fig. 2), which decreased considerably relative to the amount of the free form (peak 11) as the time of histidine starvation increased. This is understandable if the enzymes responsible for the conversion of the free form to the bound form are not biosynthesized in the absence of histidine, and probably reduced in amount due to protein turnover. We also analysed the soluble proteins labelled with ^{14}C-arginine in the absence of histidine. The incorporation of ^{14}C-arginine into soluble proteins was inhibited considerably by histidine starvation in all fractions separated by SDS gel electrophoresis (data not shown).
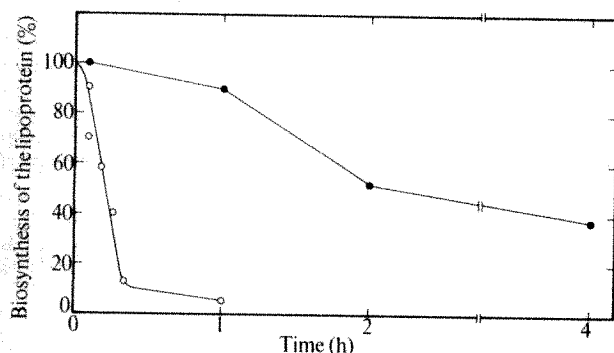
Fig. 3 Stability of biosynthesis of the lipoprotein. *E. coli* CP78 was starved of histidine as described in Fig. 2. To one of the starved culture was added 200 µg/ml. of rifampicin at zero time (○), and the other culture was incubated without the drug (●). At time intervals indicated in the figure, 15 ml. of the culture was taken, and 25 µCi of ^{3}H-arginine was added to it. The mixture was incubated for 5 min at 41° C, and chilled rapidly. The amount of the lipoprotein produced was determined as described in Fig. 2, and expressed as percentage of the amount of the protein produced in the presence of histidine between 5 and 10 min.

We have the following evidence that the protein at peak 11 produced in the absence of histidine is not due to smaller pieces of proteins of higher molecular weights[9], but is the same protein produced in the presence of histidine, that is, the lipoprotein mentioned above. (1) The unique ratio of arginine to tyrosine content of peak 11[5] was not affected by histidine starvation. (2) When the cells were starved for amino-acids such as leucine, threonine and arginine which are components of the lipoprotein, synthesis of peak 11 protein was greatly reduced, in contrast to the situation in cells starved of histidine (Table 1). (3) The exclusive biosynthesis of the peak 11 protein in the absence of histidine was also observed in another histidine auxotroph, *E. coli* 4220 (his[-]; given by Dr M. Riley). (4) The same exclusive production of the peak 11 protein was observed with a tryptophan and proline auxotroph, *E. coli* X7165 (trp[-]pro[-]; given by Dr K. Ihler).

To examine whether the protein is biosynthesized *de novo* on ribosomes, we tested the effects of well known inhibitors of protein synthesis on the production of the peak 11 protein in the absence of histidine, using *E. coli* CP78 (Table 2). Tetracycline and chloramphenicol were highly inhibitory to the lipoprotein synthesis; judging from their specificities[10], this indicates that the lipoprotein is synthesized on ribosomes *de novo*. In contrast to tetracycline and chloramphenicol, rifampicin had little effect on the biosynthesis of the lipoprotein, suggesting that mRNA for the protein is extraordinarily stable, since the present concentration of the drug used (200 µg/ml.) almost completely blocked RNA synthesis (Table 2).

Stability of mRNA for the protein was examined by measuring biosynthetic rates of the protein after the addition of rifampicin to the culture of *E. coli* CP78 starved of histidine (Fig. 3). It was found that mRNA for the protein is extra-

ordinarily stable with a half life of about 12 min in comparison with those of mRNA of other *E. coli* proteins[11-13]. Fig. 3 also shows changes in the biosynthetic rates of the protein after histidine starvation in the absence of rifampicin. After 1 h of starvation the protein was still almost fully synthesized, and even after 4 h, 30% of the full activity was maintained (Fig. 3). Since the half life of the mRNA is 12 min, one can conclude that mRNA for the protein is continuously synthesized for as long as 4 h in the cells starved of histidine. Similar synthesis of mRNA in the absence of amino-acids has been reported not only for specific enzymes such as β-galactosidase[11,15], tryptophan synthetase[12,14,16], enzymes of histidine operon[17], and acetylornithinase and ornithine transcarbamylase[18] but also for total proteins[19]. However, the amounts of mRNA produced depend on amino-acids used for the starvation[12,14,16-18].

Table 1 Effect of Amino-acid Starvation on Synthesis of Peak II Protein

Amino-acids removed	Synthesis of peak 11 protein
None	100
Histidine	100
Leucine	7
Threonine	30
Arginine	30

E. coli CP78(his[-]leu[-]thr[-]arg[-]) was starved for one of the required amino-acids as described in Fig. 2. After 5 min starvation, 25 µCi of ^{3}H-arginine was added to the cultures (15 ml.) starved for histidine or leucine, and 25 µCi of ^{3}H-leucine was added to those starved for threonine or arginine. They were incubated for another 5 min and chilled rapidly. Control experiments were carried out for both ^{3}H-arginine and ^{3}H-leucine as described above except for the presence of all required amino-acids. Envelope fractions were prepared and analysed by SDS gel electrophoresis, as described previously[7]. Radioactivities at the peak 11 position determined by DANS-internal standards[8] (Fig. 2) were measured, and expressed as per cent of those of the corresponding control experiment.

Since the protein discussed here is one of the major structural proteins of *E. coli* envelope, mRNA for the protein is possibly produced constitutively. The data reported show that this constitutive production of mRNA can continue even in the absence of histidine. It will be of great interest to examine whether such mRNA synthesis has obligatory coupling with translation of the mRNA.

We have also found that the mRNA for the lipoprotein is much more stable than mRNAs for other *E. coli* proteins. Recently we examined the stabilities of mRNAs for other envelope proteins of *E. coli*, and found that of all the major structural proteins of the *E. coli* envelope the high stability of mRNA is unique only for the lipoprotein (Hirashima and Inouye, in preparation).

Similar protein synthesis during amino-acid starvation to that we have reported here has been published for coat protein

Table 2 Effects of Inhibitors of Protein Synthesis on the Production of the Lipoprotein

Inhibitors	Production of the lipoprotein
None	100%
Tetracycline (100 µg/ml.)	2%
Chloramphenicol (100 µg/ml.)	15%
Rifampicin (200 µg/ml.)	92%

The synthesis of the lipoprotein in the absence of inhibitors was carried out as described in Fig. 2. In all experiments with inhibitors, they were added when histidine starvation was started. After 5 min, ^{3}H-arginine was added, and the mixture was incubated for another 5 min as was the control experiment. Envelope fractions were prepared, and analysed by SDS gel electrophoresis, as described previously[7]. Radioactivities at the peak 11 position determined by DANS-internal standards[8] (Fig. 2) were measured and expressed as per cent of that of the experiment without inhibitors. *E. coli* CP78 was used for all experiments.

of RNA phage f2 (histidine starvation)[20], and for tryptophan synthetase A protein (tryptophan starvation)[12,21]. In our case, only one structural protein of *E. coli* envelope is biosynthesized. This makes it possible to label specifically this lipoprotein with several unique amino-acids or amino-acid analogues without incorporating them into other envelope proteins, which is useful for structural and functional study of the protein. Furthermore, since after 4 h of histidine starvation the amount of the protein increased about three times without increasing cell mass (Fig. 3), and since the protein is metabolically very stable[5,7], it will be interesting to examine whether histidine starvation causes some distortion of the envelope ultrastructure due to the abnormal increase of the structural protein.

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L-DOPA: Effect on Ethanol Narcosis and Brain Biogenic Amines in Mice

L-DOPA augments ethanol-induced narcosis in mice[1]. Determination of brain biogenic amines suggested that the enhancement effect may be due in part to the marked increase in brain dopamine following L-DOPA administration. Here we provide further evidence to implicate dopamine in L-DOPA-induced augmentation of ethanol narcosis.

Sleeping time was defined as the length of time required for a Swiss-Webster mouse (18–23 g) to regain the righting reflex[2]. Mice were given intraperitoneal injections of ethanol (4.0 to 7.0 g kg^{-1}). Ethanol solutions were prepared at a concentration of 25% v/v, except for the 7.0 g kg^{-1} dose which was
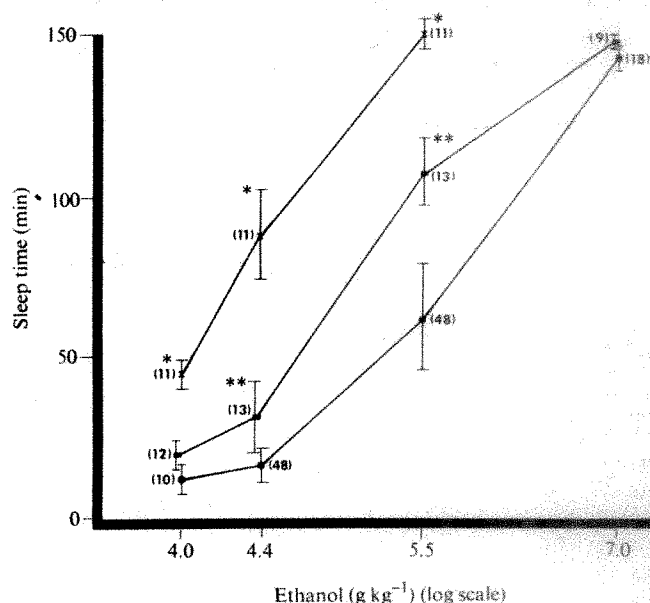
Fig. 1 Effects of acute and chronic administration of L-DOPA on ethanol-induced sleep time in mice. Standard errors of means are indicated by vertical brackets. Each point represents average data and the number of animals used in each experiment is indicated in parentheses. (*) Values significantly different from saline treatment (at least $P < 0.001$ by Student t test). (**) values significantly different from L-DOPA × 4 days (at least $P < 0.005$).
●, Saline+ethanol; ×, L-DOPA 400 mg kg^{-1} × 1 day + ethanol; ■, L-DOPA 400 mg kg^{-1} × 4 days + ethanol.

given as a 50% v/v solution so that no mouse received a volume greater than 0.75 ml. Duration of ethanol-induced sleep time was compared for groups of mice pretreated with intraperitoneal injections of saline or L-DOPA. L-DOPA methylester was dissolved in saline and administered as the free base.

Mice were given one of the following drug treatments: (1) a single administration of saline, (2) saline daily for four days, (3) a single administration of 400 mg kg^{-1} of L-DOPA, or (4) L-DOPA (400 mg kg^{-1}) daily for four days. All animals received an injection of ethanol 45 min after the last drug treatment.

Brain norepinephrine (NE) was determined by the procedure of Anton and Sayre[3] and DOPA and dopamine (DA) by the method of Merritt and Schultz[4]. Analysis of ethanol in the blood and brain was carried out in other groups of mice subjected to the same pretreatment conditions, but only 4.4 g kg^{-1} of ethanol was used. Blood and brain samples (4 mice) were taken from the three groups at their respective average duration of sleep and were analysed for ethanol[5].

Sleep times between groups 1 and 2 did not differ significantly[6], so data derived from these groups were pooled (Fig. 1). Treatments 3 and 4, before ethanol, resulted in sleep time curves which were shifted significantly (at least $P < 0.05$) to the left of the saline–ethanol sleep time curve. A single injection of L-DOPA produced the maximum augmentation of ethanol-induced sleep time. L-DOPA for four days resulted in a lesser augmentation (at least $P < 0.05$).

L-DOPA for one day showed a marked increase in both brain DOPA (192-fold, $P < 0.001$) and DA (11.1-fold, $P < 0.001$) and a lesser increase in brain NE (0.76-fold, $P < 0.01$) (Fig. 2). Similar changes have been reported by other investigators[7,8]. L-DOPA for four days resulted in an increase in brain DOPA (87-fold, $P < 0.001$), DA (3.4-fold, $P < 0.001$) and NE (1.7-fold, $P < 0.001$). Although brain levels of the respective catecholamines were increased, chronic L-DOPA significantly reduced the rise in DOPA and DA levels while increasing NE content when compared to data obtained with a single injection of L-DOPA.

Ethanol in the blood or brain after saline and ethanol did not differ significantly from that obtained after L-DOPA for 1 day and ethanol, or L-DOPA for 4 days and ethanol, despite

Table 1 Effect of Acute and Chronic L-DOPA Treatment on Blood and Brain Alcohol Levels

Treatment	Blood alcohol mg% ± s.e.	Brain alcohol mg% ± s.e.
L-DOPA 400 mg kg⁻¹ 1 day	170.3 ± 10.9	207.3 ± 17.0
L-DOPA 400 mg kg⁻¹ 4 days	216.0 ± 26.8	238.3 ± 10.4

the fact that with the single injection of L-DOPA the animals slept longer than the chronic L-DOPA group (Table 1).

L-DOPA enhanced the soporific action of ethanol in mice. This effect was reduced when L-DOPA was given for four days rather than one day. We suggest the increase in brain DA following L-DOPA indicates that the enhancement effect may be due in part to a dopaminergic mechanism, and a direct correlation exists between the intensity of the augmentation effect and the rise in brain DA level following L-DOPA. As the rise in brain DA level is reduced following chronic L-DOPA, the intensity of enhancement of ethanol sleep time is reduced.
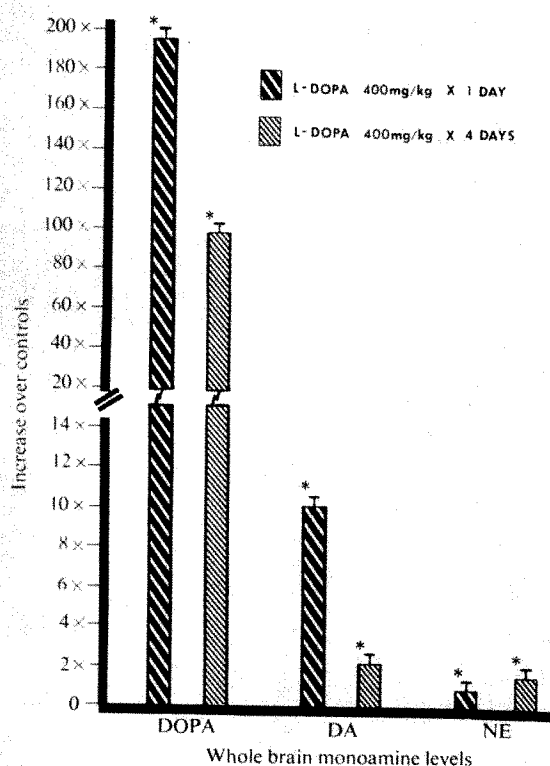
Fig. 2 Effects of acute and chronic administration of L-DOPA on mouse whole brain monoamine content. Standard errors of means are indicated by vertical brackets. Each value is an average of at least 5 determinations read in triplicate. (*) Values significantly different from saline treatment (at least $P < 0.05$ by Student t test).

The role of increased NE (0.76-fold) after the single injection of L-DOPA in the effects of ethanol appears to be quantitatively less important than increased DA (11.1-fold). Although NE increased 1.7-fold following chronic L-DOPA, enhancement of ethanol-induced narcosis was significantly reduced. Using L-DOPA to replete α-MPT-reduced stores of the catecholamines[9], it replenished NE stores, increased DA ($P < 0.05$, 60%) and partially protected the α-MPT-induced enhancement of sleep time. We suggest that DA, rather than NE, is more involved in ethanol-induced sleep.

Three groups of mice (10 each) received saline, DA (10 mg kg⁻¹) or disulfiram, a beta hydroxylase inhibitor (400 mg kg⁻¹). Ethanol (4.0 g kg⁻¹) was injected with saline or dopamine, or four hours after disulfiram or saline. DA, observed
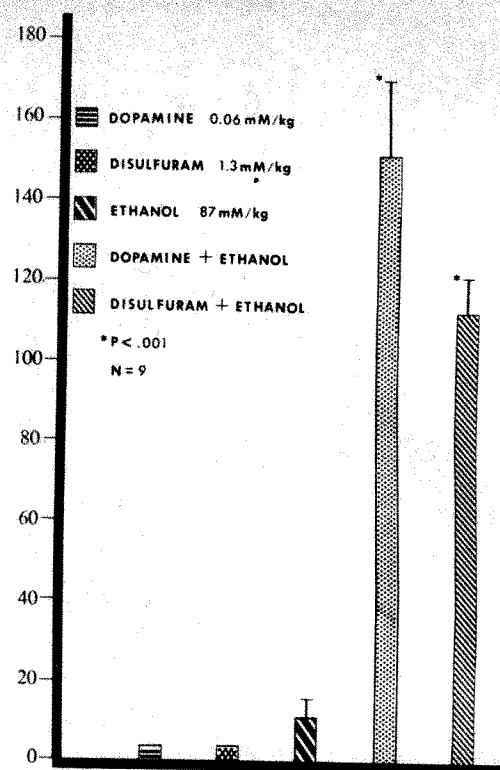
Fig. 3 Effects of dopamine and disulfiram on ethanol-induced sleep time in mice. Nine mice divided into three groups received saline, DA (10 mg kg⁻¹) or disulfiram (400 mg kg⁻¹). Ethanol (4.0 g kg⁻¹) was injected with saline or dopamine, or four hours after disulfiram or saline. Standard errors of means are indicated by vertical brackets. (*) Indicates values significantly different from saline treatment ($P < 0.001$).

previously[10], and disulfiram treatment potentiated ($P < 0.001$) sleep time induced by ethanol (Fig. 3). Disulfiram reportedly decreased brain NE by 56% and increased DA by 14%[11]; in our experiment, it produced a temporary increase in the ratio of DA/NE resulting in DA > NE and the accompanying enhanced ethanol-induced behavioural depression. The synergistic action of disulfiram, however, may be due to its effect on aldehyde dehydrogenase[12]. Our results indicate that L-DOPA induced enhancement of ethanol sleep is due to the rise in brain DA.

L-DOPA is converted by a pyridoxal phosphate-dependent decarboxylation reaction to DA[14] and reacts with pyridoxal phosphate *in vitro*[15]. Removal of pyridoxal phosphate by chronic L-DOPA possibly lessened decarboxylase activity with a decreased conversion of DOPA to DA. Diminished formation of DA, however, may be due to decreased brain L-DOPA uptake.

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Binding of Concanavalin A to the Surface of Unfertilized and Fertilized Ascidian Eggs

STUDIES with certain carbohydrate-binding proteins of plant origin (as concanavalin A and wheat germ agglutinin) have indicated that some surface properties of embryonic[1,2] and of virally transformed cells[3-6] are different from those of adult cells. The interpretation of the differences in terms of structural organization of the cell surface is, however, still controversial (see for example refs. 7 and 8).

We have used concanavalin A (Con A) as a tool to explore the changes taking place in the surface of the Ascidian egg in conjunction with fertilization. Indeed, while it is well documented by studies both at the morphological and the physiological level (see ref. 9 for a review) that fertilization brings about an extensive reorganization of the egg surface, whether and to what extent these changes are relevant to the onset of development or only to the process of sperm-egg interaction is not known.

In this paper we show that in the Ascidian egg at the time of completion of maturation (which coincides with the reacquisition by the egg of the ability to divide) a dramatic change occurs in the detectability of Con A binding sites on the egg surface.

The choice of the Ascidian egg to explore the changes of the egg surface at the time of fertilization by the use of molecular probes was dictated by the following considerations. The Ascidian egg is among the few eggs well suited for microscopical analysis (the eggs of the Mediterranean species are very transparent and have a diameter of about 100-140 μm) whose chorion can be manually removed, thus exposing a naked egg surface; neither by conventional electron microscopy nor by staining with ruthenium red can an extracellular coat be detected. This is an essential prerequisite for use of molecular probes to provide meaningful information about the cell surface.

In the Ascidian oocyte, the meiotic process is arrested at the metaphase of the first division and is only resumed following fertilization. Within 20-30 min after fertilization, meiosis is completed and the two polar bodies are ejected. The male and female pronuclei then merge in the zygote nucleus and soon afterwards the egg undergoes the first cleavage. Immediately following fertilization, the egg surface appears to be stretched at the animal pole and to contract at the vegetal pole (which is the site of sperm entry)[10]. At the same time the egg becomes sensitive to taurocholate-induced cytolysis[11].

Rapid cytoplasmic movements also follow fertilization; they cause the egg to undergo amoeboid-like deformations[12]. After the ejection of the second polar body, these movements lead to the segregation of cytoplasmic components into specific areas and eventually into the blastomeres from which the different cell lines originate[13].

We have used eggs of *Ascidia malaca* and of *Phallusia mamillata* collected from the gonoducts; the chorion was removed with tungsten needles under a dissecting microscope.

Fluorescein isothiocyanate-conjugated Con A (a gift of Dr L. Sachs, the Weizmann Institute) was diluted in seawater to a final concentration of 70 μg ml.$^{-1}$. Eggs and cleavage stages stained with fluorescent Con A often underwent cytolysis during observation if a seawater-glycerol mountant was used. This could be prevented by a 10-min fixation in isotonic 3% neutral formaldehyde in seawater. The eggs, both fixed and unfixed, were stained for 10 min and rinsed in seawater before observation. Comparison with unfixed material showed that fixation did not alter Con A binding. For the observation of fluorescence a Zeiss Universal microscope was used with an Epicondensor and standard ultraviolet filters for fluorescein. The eggs of *A. malaca* are slightly autofluorescent, but negligibly so when compared with the stained specimens. *Phallusia* eggs, however, showed considerable autofluorescence near the wavelength of fluorescein emission; for this reason most of our observations were done with *A. malaca* eggs. Agglutination tests were performed with Con A (Calbiochem) in concentrations of 50 to 500 μg ml.$^{-1}$ in seawater.
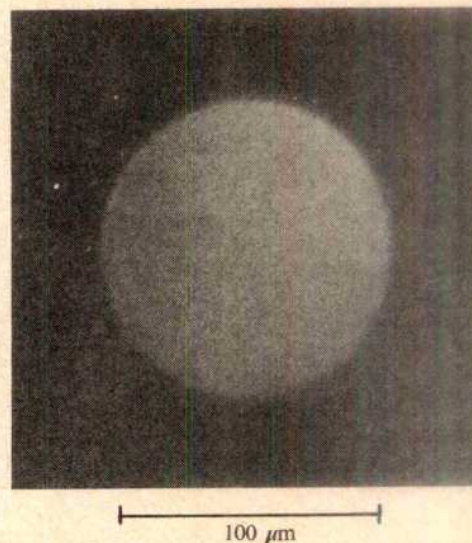
Fig. 1 Unfertilized egg of *Ascidia malaca* treated with trypsin and then exposed to fluorescein-conjugated Con A.

Unfertilized eggs of *A. malaca* are not agglutinated by Con A at these concentrations and no binding of fluorescent Con A is observed. A slight degree of agglutination is exhibited by the unfertilized eggs of *Phallusia*; however, the clumps are readily dispersed on gentle shaking of the dishes. Until the ejection of the second polar body, no Con A binding can be detected either by the agglutination or by the fluorescent test. However, a 30-min treatment with 0.1% Trypsin (Worthington) results in agglutination when the eggs are subsequently exposed to a 50 μg/ml. solution of Con A; also, binding of fluorescent Con A becomes detectable (Fig. 1). In the case of the *Phallusia* eggs, the clumps of trypsin-treated agglutinated eggs do not disperse on shaking of the dishes.

Immediately following the ejection of the second polar body, Con A strongly agglutinates the eggs in clumps that are not dispersed by shaking the dishes. The sudden appearance of agglutinability is most strikingly demonstrated when eggs are exposed to a 50 μg ml.$^{-1}$ solution of Con A at any time

between fertilization and the formation of the second polar body; indeed the maturation process continues in the presence of Con A and the eggs do not show any tendency to agglutinate. As soon as the second polar body has been given off, agglutination immediately occurs. Concurrently, treatment with fluorescent Con A results in the appearance of a bright fluorescence (Fig. 2), which is in fact brighter than that of the unfertilized eggs treated with trypsin. Both agglutination and fluorescence are abolished by α-D-methyl-manno-pyranoside, showing that they are due to the specific binding of Con A to its receptor sites[14].

|—————— 100 μm ——————|
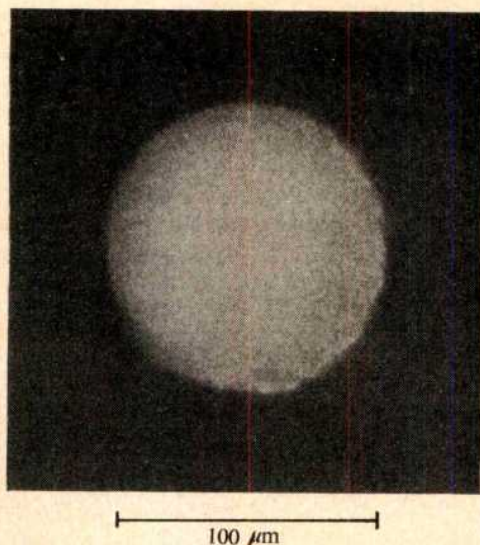
Fig. 2 Egg of *Ascidia malaca* exposed to fluorescent Con A immediately after the ejection of the second polar body.

We interpret these observations as indicating that, in the Ascidian egg, completion of maturation is accompanied by a molecular rearrangement of the egg surface. Quantitative estimates of the Con A binding sites before and after the ejection of the second polar body are in progress. Hence for the time being we cannot say whether our results are due (1) to an all-or-none exposure of the Con A binding sites, or (2) to an increase of the available sites, or (3) to their topological rearrangement (see refs. 5, 6 and 15). The following points are pertinent to the interpretation of our observations.

Table 1 Changes in Diameter of the Eggs of Four *Ascidia malaca* at the Time of Fertilization

Experiment No.	No. of eggs	Unfertilized eggs Diameter (μm)	σ	After ejection of second polar body Diameter (μm)	σ
1	8	112.4	0.02	109.7	2.09
2	10	106.2	0.52	103.7	1.31
3	21	107.9	<0.001	107.3	0.13
4	4	109.2	0.64	107.9	<0.001

There is a small variability in size not only among the eggs of different animals but also among those from the same animal, so the data in the table have been computed from the measurements of the diameter of individual eggs before fertilization and after the ejection of the second polar body.

(1) Since it is known that the eggs of some animals undergo a marked shrinkage on fertilization[9,11], the possibility should be considered that the appearance of fluorescence and of agglutinability may be due to a clumping of previously scattered Con A binding sites. This, however, is made unlikely by the data in Table 1 which show that while the eggs of some animals do not undergo any change in size after fertilization, in other

cases only a slight decrease occurs. Furthermore, it seems that, when all the eggs are considered together, in 65% of them no change in diameter after fertilization can be detected; a decrease of between 3.6 and 4.1% occurs in 30% of the eggs; and only in 5% of the eggs is the decrease of about 7%. We conclude that such size changes, even when they take place, are too small to account for a shrinkage-dependent clustering of the Con A binding sites.

(2) The fact that Con A binding sites become detectable by the use of fluorescent Con A at the surface of the unfertilized egg as a result of trypsin treatment suggests that at least one part of the sites is in a cryptic condition. It is interesting that neither of the changes that occur at the egg surface immediately after fertilization, namely the sensitivity to taurocholate[11] and the surface movements[10], involves exposure of the Con A binding sites. This means that it is only after maturation has been completed that the molecular architecture of the egg surface is altered in such a way as to permit detection of the Con A binding sites (at least by the methods we have employed). Whether or not this cell surface change is causally related to the resumption by the egg of the ability to replicate its DNA and to divide cannot be decided on the basis of the present experiments. Preliminary observations indicate that no further changes in the cell surface occur with respect to Con A binding in the course of cleavage.

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Hormonal Pregnancy Tests and Spina Bifida

GAL[1] has suggested that hormonal pregnancy tests may be teratogenic to the developing central nervous system. In a study of 100 mothers of spina bifida cases she found nineteen of these

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mothers had had a hormonal pregnancy test ('Amenorone Forte' or 'Primodos') compared with four of 100 "matched" control mothers. Laurence[2] has criticized Gal's findings on two counts: (1) the choice of controls, and (2) the possibility of finding a difference this great by chance when a number of epidemiologic factors are studied.

An examination of the data presented by Gal[1] suggests an important factor in the pathogenesis of spina bifida may have been overlooked. Gal states that the average interval between conception and pregnancy test was 5.6 weeks for the survey group and 6.2 weeks in the control group. If the index cases were open lesions of the spine (myeloceles or myelomeningoceles), which are the most common forms of spina bifida, these would develop during the first phase of neural tube formation[3]. The neural tube is formed and closed by 28 days gestational age[3] so any teratogenic factor would need to be operating before this time. The average interval between conception and pregnancy test in the study group was 5.6 weeks, implying that a large proportion of these mothers received the hormones after a teratogen could affect the closure of the neural tube, that is, after the 4th week. For Gal's findings to be biologically significant, the time of operation of the proposed teratogen must be more precisely established and be before the closure of the neural tube.

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Spatial Frequency Dependent Chromatic After-effects

McCollough[1] first reported that following prolonged inspection of vertical gratings on orange backgrounds successively alternating with horizontal gratings on blue backgrounds, the vertical stripes in an achromatic test pattern will appear greenish and the horizontal stripes will appear pink. Because the effect was evidently related to the orientation of the grids on the retina, McCollough hypothesized that it was due to adaptation or fatiguing of colour- and orientation-specific edge detectors in the visual system. But recent studies[2-4] employing two grids of varying spatial frequency but with the same orientation have demonstrated similar chromatic after-effects on achromatic test patterns of the same orientation.

My studies examined the interdependence of spatial frequency and orientation-specificity of chromatic after-effects. It was hypothesized that chromatic after-effects could be produced with stimulus attributes totally independent of orientation.

Six subjects who were familiar with the McCollough effect but were naive with respect to the hypothesis of my experiment viewed two black horizontal gratings with a spatial frequency of five cycles/degree and 10 cycles/degree respectively. The narrow gratings were projected through green filters (Wratten 52), the wide gratings through magenta filters (Wratten 34A). The 35 mm slides were viewed binocularly through a projection tachistoscope; the image was projected on ground glass by two Kodak carrousel projectors. The 40 training trials consisted of alternate presentations of the slides for 7 s with a dark interval of 5 s. Five minutes after this training period, subjects viewed a variable spatial-frequency grid, ranging from 2 to 20 cycles/degree projected on a white screen. Half saw this test grid in a horizontal orientation first; the other half saw it in a vertical

orientation first. The grid was then rotated 90°. Subjects were asked to report any colour effects observed in either or both orientations. If an effect was observed, subjects were instructed to locate the point of maximum chromatic saturation on the grid. They were also asked to compare the strengths of the effects at this point of maximum saturation in the two orientations.

All subjects reported a greenish tint on the narrow-spatial frequency portions and a reddish tint on the wide-spatial frequency portions for both orientations of the test grid, with an achromatic band between the two sections. The effect was strongest near the spatial frequency which corresponded to that of the training slide. Subjects reported a decreased (desaturated) effect as the spatial frequency deviated in either direction from that of the training grids. Qualitatively, they judged the strength of the effect to be similar in both orientations.

In a second experiment, the training procedure was identical, except that the training stimuli were concentric circles, one with a spatial frequency of 5 cycles/degree and the other 7.5 cycles/degree. The test stimulus consisted of a series of 22 concentric circles varying in spatial frequency from one cycle/degree at the centre to 15 cycles/degree at the periphery. Five subjects from the previous experiment and three new subjects participated in this experiment. Half viewed the narrow circles through red and the wide circles through green filters, and the order was reversed for the other subjects. A five minute interval separated the training and test phases. Subjects were instructed to report colour effects on the test pattern and to indicate the region of maximal saturation.

All subjects reported colour bands extending around the entire circumference of the circles. Those who had viewed narrow green circles and wide red circles reported a reddish or pink tint on the narrowly spaced portion and a greenish tint on the widely spaced portion of the test pattern. Analogous after-effects were reported by those subjects who had viewed the alternately paired training stimuli. Three experienced subjects commented that the effect was considerably weaker than those observed in the previous experiment.

The results of both experiments argue in favour of independently functioning channels for the processing of orientation and spatial frequency attributes of visual stimuli. These findings suggest that explanations based on the response characteristics of single units become increasingly less parsimonious. Orientation specificity is a defining characteristic of edge detectors and to a lesser extent seems to apply to size detectors as well[5,6]. Parker[7] argued for the existence of a class of neurones with orientation specific tuning but responding to a range of spatial frequencies. The present findings would require yet a further class of units which are spatially tuned but nonspecific with respect to orientation. To account for the chromatic aftereffects, units in each of these classes would also have to be tuned to specific wavelength band, become "fatigued" as a result of prolonged stimulation as in the McCollough effect, and produce complementary responses.

It seems that no explanation of the effect based on a single neural unit can be adequate. Both line orientation and spatial frequency seem to be sufficient but not necessary stimulus attributes to produce an after-effect. A more adequate, yet physiologically nonspecific, model can be developed from these and other findings. I propose that an association occurs between some attribute of the stimulus structure, for example, orientation, and the chromatic characteristics of the training stimuli. Because the after-effect appears as a hue approximately complementary to the hue of the training stimuli, an association between the structural aspects and an opponent colour response must occur. A learning model analogous to classical conditioning appears to have considerable heuristic, if not explanatory, value. Physiologically it may be speculated that chromatic information is relayed to cortical centres via neural units in the lateral geniculate nuclei which respond in a manner consistent with an opponent process[8] to form an

association with the contour related information processed by appropriate cortical neural units.

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The Role of Contours in Stereopsis

JULESZ[1] showed that the presence of monocular patterns or familiar shapes is not necessary for stereopsis and that correlated noise matrices presented binocularly can yield vivid depth effects. Random dot stereograms "demonstrated that stereopsis not only can occur without monocularly recognizable shapes but actually does occur. That is, if monocular shapes exist then stereopsis precedes their recognition . . .[2]". Julesz also suggested that stereopsis may result from simple point to point matching[3] of the left and right eye fields. Experiments with random letter stereograms[4] and gratings[5] emphasized the importance of brightness gradients in stereopsis and Kaufman concluded that "subjective contours" are not sufficient to produce stereopsis.

The problem is: what features of a pair of patterns can define the disparity that gives rise to the perception of stereopsis? We investigated whether disparity of visual texture is sufficient in itself to produce stereopsis using Fig. 1.

Pickett[6] found that (in random dot matrices) texture discrimination can occur if the density of elements (first order of probability) is kept constant and the tendency for like elements to occur in "runs" (second order of probability) is varied, in spite of there being no differences in average intensity. We constructed stereogram 1 (Fig. 1) using a "texture discrimination" pattern from a publication of Pickett[6]. Discrimination of nasally displaced inner square in each half image is based on a difference in second order statistics alone.

We found that the brain can discriminate textures such as those shown in Fig. 2 based on granularity or size of the dots. In stereogram 2 (Fig. 2) the patterns are random "noise"; the outer area in each half image is simply the enlarged version of the inner nasally displaced texture. As both white and black elements are equally enlarged to produce the outer areas, the average intensities of outer and inner areas are equal. In spite of this, discrimination is possible.

In both these stereograms the two half images are com-

Fig. 1 Texture disparity stereogram. Texture discrimination based on differences in second order statistics.
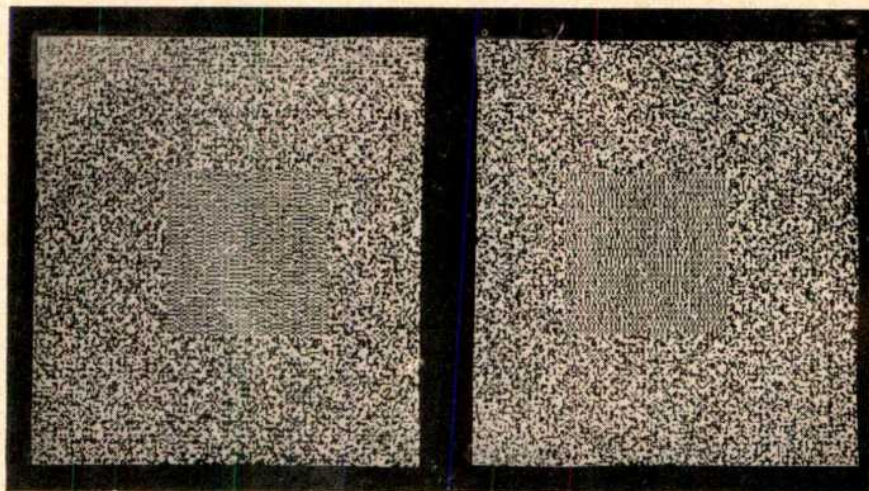
Fig. 2 Texture disparity stereogram. Texture discrimination based on size of grain. This is an inaccurate version of the original stimuli used in our experiment. In the original stereogram all intensity contours were eliminated using white paint and appropriate illumination.
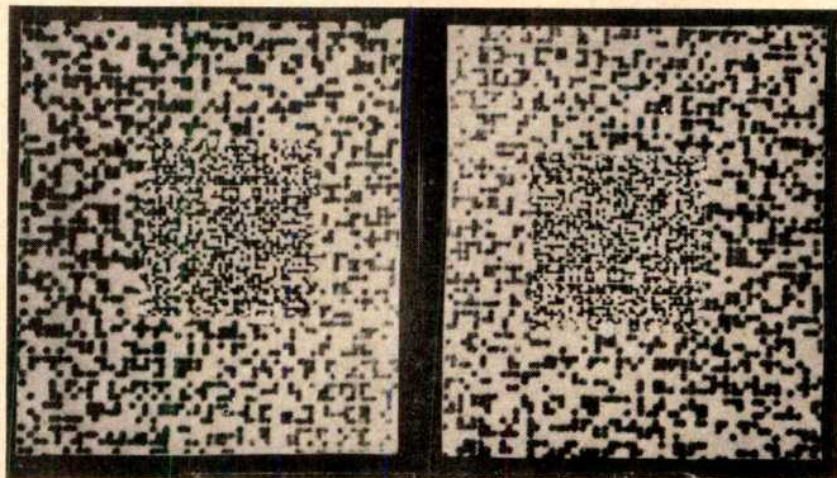
a   *b*

Fig. 3 Disparity of subjective contours formed by grating direction change
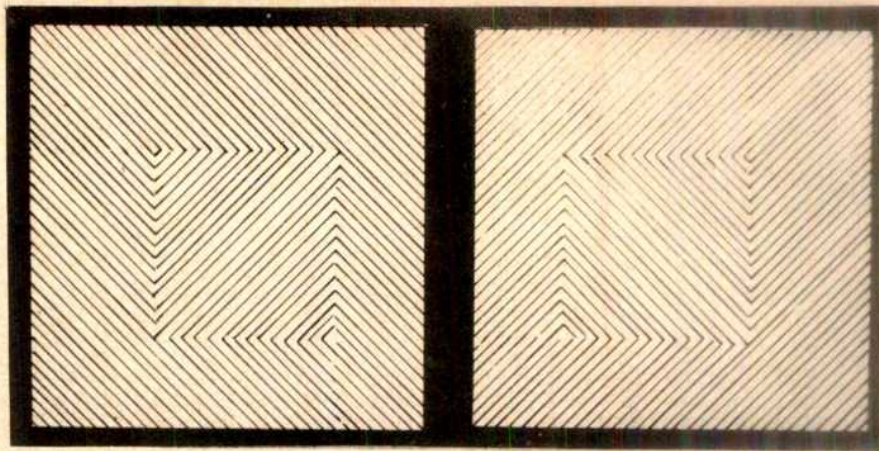
pletely random uncorrelated noise. The spatial distribution of dots in one half image has nothing to do with the spatial distribution of dots in the other half image. In each half image, however, there is a discriminable central patch shifted nasally. Are the discrimination and disparity of such abstract "gestalt contours" as these sufficient for stereopsis, although with respect to dot distribution, pattern *a* has no point to point correlation with pattern *b*?

Stereograms (Figs. 1 and 2) with nasal and temporal disparities were presented in random order to 6 trained 0's (20 trials for each 0) and they were provided with zero disparity "controls" for comparison. All 0's reported stereopsis with Fig. 1 in the correct direction for 100% of trials. The accuracy was 95% for Fig. 2 (but the "quality" of stereopsis was poor).

front of or behind that of the outer square. This result is of particular interest, for it suggests that there might be a common contour processing mechanism in the brain for both subjective "texture" contours and intensity contours.

In Fig. 3 there are subjective contours formed by grating direction change. All 6 0's reported stereopsis in the correct direction for 100% of trials when presented with crossed and uncrossed disparities in random order for 20 trials each. Kaufman's negative result[5] with similar stereograms could probably be explained by the fact that the disparities he used were too small (for the grating band-width which he used).

Treisman[7] and Julesz[3] have shown that colour can provide a cue for stereopsis. This seems to be true even in the absence of point to point correlation between two half

Fig. 4 Disparity of subjective contours formed by Vernier resolution.
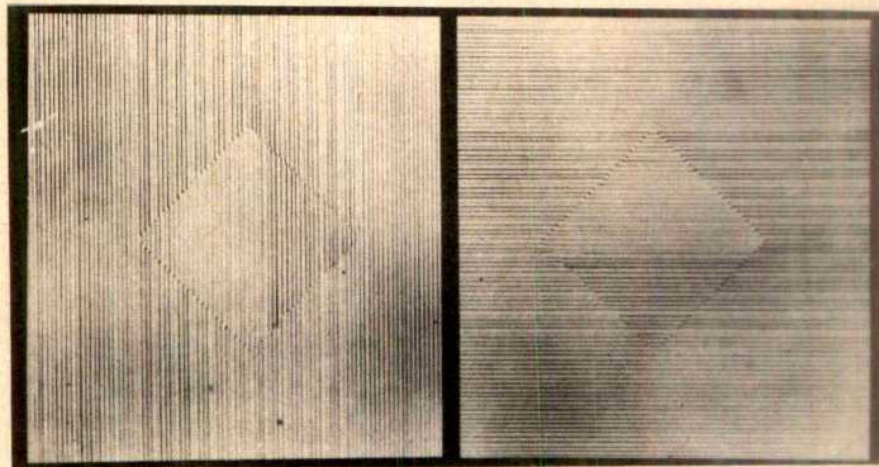
This result is all the more surprising in view of the fact that in "noise" patterns presented binocularly each dot in the left eye usually selects the nearest available partner dot from the corresponding area of the other eye for fusion and yields stereopsis depending on the disparity of the selected partner dot. In the absence of other cues proximity seems to be the cue for stimulus selection in stereopsis. Why does the proximity rule fail when subjective contours are presented in noise patterns?

We also presented a "texture contour" such as the one used in Fig. 1 to the left eye and an intensity contour (formed between a light grey surround and dark grey inner square) to the right eye. Stereograms of this type with crossed and uncrossed disparity were presented in random order 20 times to each of 6 trained 0's. Accuracy of reported direction of depth was 100% for three of the 0's, 90% for two of the 0's and 70% for one. The combined image was reported to be diplopic, rivalrous and unstable, but the border of the inner square was clearly either in

images[8]. In Fig. 4 one half image consists of a dark grey outer area and a light grey nasally displaced inner area. In the other half image the outer area is red and the inner area is green (Wratten Green Filter No. 58). The intensity of the inner green area was varied gradually over a wide range using a pair of polaroids. At some setting, at least, the intensities of the outer and inner areas must have been equal, thereby eliminating incidental intensity gradients. Yet none of the 3 0's who viewed the stereogram reported disappearance of stereopsis at any point, showing that a "pure" colour contour can produce stereopsis with an intensity contour. The same set-up was used with colour contours presented to both eyes to show that "pure" colour contours can interact binocularly to produce stereopsis (The intensities of the green areas in the 2 half images were varied synchronously.)

The validity of Julesz's model for stereopsis as far as correlated patterns are concerned cannot be doubted[1-3]. As in our stereograms (Figs. 1 and 2), however, the half images

are completely uncorrelated "noise", Julesz's model is inapplicable. Further, Kaufman's brightness averaging hypothesis[4,5] cannot be applied to our patterns (Figs. 1, 2 and 3) as "brightness averaging" could have resulted only in a uniform grey field in each eye.

It seems likely from our results that even the most "subjective" of subjective contours can yield depth effects in the absence of average brightness gradients and point to point correlation. Texture discrimination based on probability distributions (Fig. 1) and size of grain (Fig. 2) and the recognition of contours formed by changes in grating direction (Fig. 3) all occur "earlier" than stereopsis and considerably influence it. Any model that tries to "explain" stereopsis must take these facts into account. Our experiments also emphasize the importance of using random dot stereograms in perceptual research, for only by using Julesz patterns can one "skip" peripheral preprocessing (of the type seen in Figs. 1, 2 and 3) to obtain a truly cyclopean "counterpoint".

From our finding that a texture contour or a colour contour presented to one eye can produce stereopsis with an intensity contour presented to the other eye, we postulate a common contour processing centre for intensity, colour and texture contours where parallel inputs become confluent into a single channel. Sherrington postulated[9] over 60 years ago "that during binocular regard . . . each monocular mechanism develops independently a sensual image of considerable completeness. The singleness of binocular perception results from union of these elaborated uniocular sensations". Our results strongly support this important conclusion.

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Locomotion and Burrowing in Limbless Vertebrates

GAYMER[1] recently described "vermiform" movement as a fifth[2,3] and "new" method of locomotion in limbless terrestrial vertebrates. On the basis of X-rays of limbless amphibians (caecilians) he stated that these animals can shorten their bodies by flexing the vertebral column into multiple curves of short radius within the integumentary envelope. The shortened region is apparently fixed against the soil or tunnel walls and the head then moves forward from this stationary zone. The fixed region thus serves in force transmission to the soil, allowing the animal to pull up its posterior trunk, or send the anterior portion further along the path. Gaymer noted that the fixed zone thus formed may also serve as a base for ramming movements.

The shortening and thickening of the caecilian trunk by axial flexure have been known, if inadequately understood, for some decades[4]. Indeed, vermiform locomotion superficially resembles the movement of annelids, where part of the trunk is thickened and placed in static frictional contact with the walls of the tunnel. Forces transmitted here can move the body along a tunnel or let the animal push its way through the ground. These properties of vermiform motion are, however, those that characterize powered concertina movements, supposedly a distinct category[2,3]. The difference between the usual concertina and vermiform forms of locomotion is that while the entire body flexes in the former, flexion is restricted to an axial mass in the latter so that the supervening soft tissues swell outwards. Thus vermiform locomotion is a variant of the concertina locomotion of limbless vertebrates; it is not a distinct method.

Gaymer's description of vermiform locomotion argues that such a pattern could not be developed in reptiles because their ribs extend into the body wall muscles close to the skin. However, this variant occurs in a number of limbless reptiles. Thus the slender and bilaterally compressed amphisbaenian Agamodon compressum uses it in tunnelling through packed sand. In the Uropeltidae, a relict family of snakes restricted to Central India and Sri Lanka (Ceylon)[5], this method is most highly developed; it is used not only in progression and ramming but also in tunnel widening. The anterior part of the body can, by flexion of the vertebral column, be thickened to more than twice the normal diameter. In this case the basic concertina mechanism facilitates tunnel formation. The tiny head is driven in only to the level of the neck and thus serves primarily for the initial penetration. Widening of the tunnel to full diameter occurs by flexion between the anterior vertebrae, so that the penetrating and the widening functions are separated[6].

Finally, Gaymer states that "the skin of reptiles is largely free from the underlying muscles for part or all of the body's circumference, being attached only by specially developed cutaneous muscles".

Amphisbaenians and such snakes as uropeltids do indeed have cutaneous muscles (that is, those cross-connecting different portions of the skin[7]), but these are not involved in the propulsion phase of rectilinear movement, which is enabled by slips of the axial musculature (Mm. costocutanei superiores and inferiores[3,8]). In concertina, propulsive forces pass directly from the independently flexed vertebral column to the loosely connected skin. Behavioural evolution, coupled with only slight structural changes, accounts for repeated and varied development of concertina locomotion in reptiles.

Internal concertina is produced differently in squamates and caecilians. In uropeltids most bones, axial muscles, and viscera flex within an envelope consisting of the skin and cutaneous muscles. In caecilians the flexure is restricted to a central zone occupied by vertebrae, ribs, and spinal musculature (epaxial+ hypaxial?)[4]; the remaining axial musculature has become attached to the body wall.

The slender slips of muscle may reposition the skin; they do not transmit the propulsive forces which pass in static contact from column to skin to tunnel wall. The reinforcement of the wall may protect the visceral contents in a short-ribbed, elongate burrower.

Gaymer argued that the caecilian morphology was shaped by the need for internal curvature. Actually the separation between axial and body wall muscles maintains the patency of the visceral cavity by muscular rather than by skeletal elements.

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Trophical Role of Bacteria in the Ecosystem of the Coral Reef

THE factors responsible for the high productivity of coral reefs in oligotrophic tropical waters are still not understood[1,2]. The relative importance of the predatory and symbiotically herbivorous nutrition of corals is not clear[3], and other feeding microscopy on stained membrane filters. The rates of bacterial production and bacterial destruction and of photosyntheses of phytoplankton and phytobenthos and a quantitative study of the feeding of aquatic animals with bacteria have been made using carbon-14[8-11]. Some of my main results are summarized in Table 1 as quantitative estimates of the microflora in the water, bottom sediments and epibiotic layers covering dead corals.

The biomass and the production of bacteria are of the same range as those in a eutrophic or a mesotrophic lake[12], and several tens or even hundred times more than that in the pelagic regions of the ocean. The rate of destruction of organic matter usually exceeds the rate of primary production in the surface layers of water and sediments. The organic matter of microbial cells itself accounts for about 2–5% of the total organic matter of the reef sediments. The daily rate of bacterial production in sediments is usually around 30–60% of the photosynthetic production of phytobenthos and results in a daily production of raw bacterial biomass in the reef sediments of about 5–15 g/m² of the bottom surface.

The high rate of bacterial production may provide a significant part of the food of the very rich fauna of the coral reefs, which includes the filtering and the sand and detritus-eating animals. The latter groups include a part of the coral fishes. The experiments with ^{14}C-labelled bacteria as a food showed that most of the common reef filter feeders can feed on bacterial plankton at concentrations equal to those in the lagoon water (Fig. 1). The consumption of bacterioplankton by crude filter feeders such as tunicates, oysters, and crustaceans is facilitated

Table 1 Quantitative Estimates of Bacterial Biomass, and Daily Values of Production of Bacteria, Photosynthetic Production and Destruction* in Coral Communities

Sampling area	Type of samples	Bacteria Biomass (B)	Bacteria Production (P)	Photo-synthesis (ph)	Destruction (D)	P/B	D/ph
Open ocean, north trade wind current	Bottom sediment, red clay	1.0	0.032	—	0.08	0.03	—
	Surface water	1.7	2.6	0.51	6.9	1.6	13.6
Fanning Atoll, Line Island	Coral sand	91	22.6	38	56	0.25	1.5
Great Barrier Reef, close to Heron Island	Coral sand	42.5	27.6	61	69	0.61	0.85
	Water over the reef	41	20.2	67	53	0.49	0.79
Majura Atoll, Marshall Islands	Dusty fine sediment among dead corals	88	35.2	74	100	0.40	1.4
	Epibiotic layer on the dead corals	28	14.3	610	41	0.51	0.06
	Coral sand	21	7.2	20	20	0.34	1.0
	Water over the reef	19	7.5	4.1	21	0.39	5.1
Kaneoche Bay, Oahu Island, Hawaii	Coral sand	65	17.2	7.1	49	0.26	6.7
	Seston over the surface of dead corals	147	73.0	96	207	0.50	2.2
	Water over the reef	43	28.0	36.3	79	0.67	2.2
Butaritari Atoll, Gilbert Islands	Water near the shore	170	41.5	37	110	0.24	3.0
	Water in the centre of lagoon	79	24	17	64	0.30	3.7

* mg C l.$^{-1}$ of raw sediment, or mg C m^{-3} of water.
Variation range between parallel duplicates: primary production 20%, microbial production in surface samples and shallow sediments 15%, deep sea samples 50%.

mechanisms, filtering and osmotic nutrition[4,5], have not been studied sufficiently. Furthermore, very little is known about the microbial population of the reef ecosystems. Di Salvo[6] showed that reefs support an abundant and active microflora which participates in nutrient regeneration and serves as food for filter feeders including some corals[7], but there are no quantitative data relating to the biomass and production of microflora on reefs.

I collected data at several atolls in the Pacific Ocean during 1968–1970. Microbial biomass has been determined by direct by the presence of about 20–30% of the total bacterioplankton in aggregates larger than 5 μm[11]. Sand and seston eaters also consume and assimilate labelled bacteria in the sediments (Fig. 2).

Several series of experiments with corals were also carried out. The common corals (Porites, Pavona, Hydnophora, Montipora, Fungia, Porcillopora sp.) were fed with the labelled natural bacterioplankton and seston, in which the bacterial population was labelled with ^{14}C. The evolution of labelled metabolic CO_2 by corals previously fed with labelled bacterio-

plankton, and then transferred into clean unlabelled seawater, was accepted as a measure of the intensity of feeding and digestion of labelled bacteria. All the corals tested were able to feed and digest the bacterial plankton (Fig. 2, Table 2) at concentrations close to that in the lagoon (Fig. 1). My data confirm Di Salvo's[7] results and indicate the importance of careful studies of the filter feeding coelenterates.
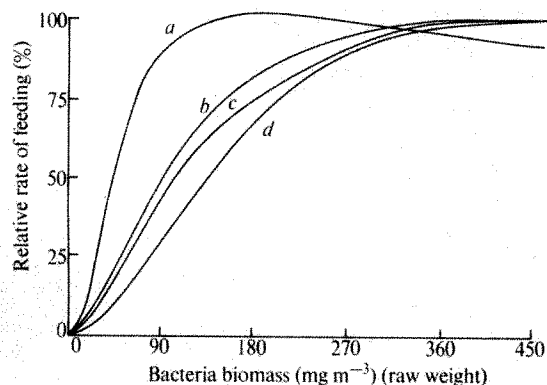
Fig. 1 Dependence of feeding rate upon the concentration of bacterioplankton for some common reef filtering animals. a, Sponge *Toxadocea*; b, veligers; c, oyster *Grossostrea*; d, coral *Pocillopora*.

Sections made off the lagoons of atolls and off barrier reefs into the open sea showed that the influence of the eutrophic coral communities upon the productivity of the surrounding blue oligotrophic tropical waters usually detected only in the shelf zone at a distance of 10–15 km from the reef (Fig. 3).
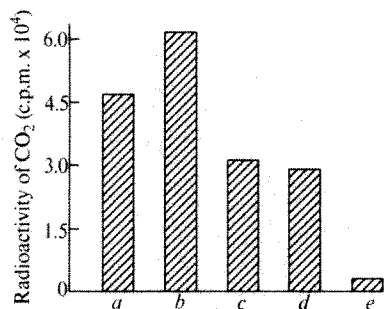
Fig. 2 The evolution of labelled CO_2 (in c.p.m. $\times 10^4$) by corals after exposure in seawater with ^{14}C-labelled bacterioplankton, and 2 h subsequent exposure in unlabelled water. The specific activity of the experiment was 35–40 g. a, *Pocillopora damicornis*; b, *Montipora verrucosa*; c, *Porites compressa*; d, *Fungia scutatia*; e, control (formalin).

These data demonstrate the important role of the bacterial population in the metabolism and productivity of the reef ecosystem. Its "internal" function is that of nutrient regeneration, and of the production of particulate protein food at the expense of the energy of mineralization of dead organic material. The "external" function of the bacterial population of coral reefs may lie in the consumption and accumulation of external energy, the energy of the organic matter contained in the oceanic waters passing over the reef. Surface oligotrophic tropical waters contain labile organic matter[11], which is mainly dissolved, and can be consumed by the rich epibiotic microflora which covers great areas of the surfaces of reefs, dead corals and sediments[13]. Further studies may help to evaluate the
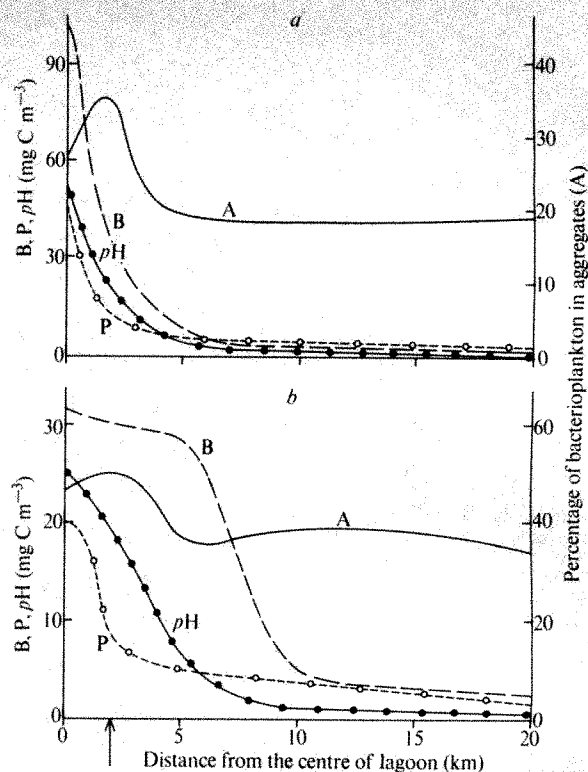
Fig. 3 The changes of biomass (B), daily production of bacteria (P) and photosynthesis (ph), % of bacterioplankton in aggregates (A) at two cross sections. a, From the centre of the lagoon at Tarawa atoll; b, off Heron Island (Great Barrier Reef) to the open sea. The arrow shows the break in the outer reef.

sources of the extra organic matter necessary to cover the excess of destruction over primary production in the reef communities, and to solve the enigma of the high productivity of these most interesting marine ecosystems.

Table 2 Daily Ration* and the Ratio % of Assimilated to Consumed Food † Determined by Feeding Common Reef Animals with Bacteria

Animal	R (%)	C (%)
Gastropod veligers	51.0	61
Hydroid, *Pennaria tiarella*	43.5	74
Annelid, *Serpullidae* sp.	7.8	73
Coral, *Pocillopora damicornis*	5.5	76
Coral, *Montipora verrucosa*	5.8	82
Sponge, *Toxadocea violacea*	3.4	82
Tunicate, *Ascidia nigra*	1.6	83
Holothurian, *Ophiodesoma spectabilis*	10.4	22
Gastropod, *Nerita picea*	9.4	20
Lamellibranch, *Grossostrea gigas*	2.2	68

* As % of the total body organic matter (R).
† Conversion, C.

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Inhibition of Monoamine Oxidase by the Pesticide Chlordimeform and Related Compounds
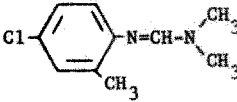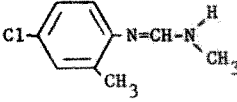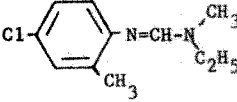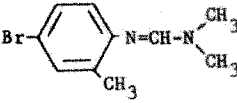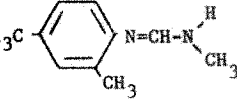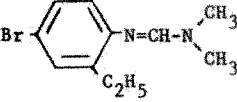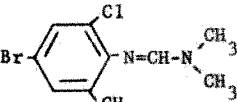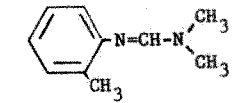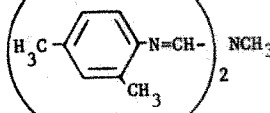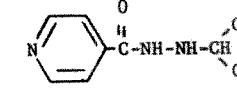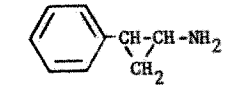
CHLORDIMEFORM is a formamidine acaricide and insecticide used to control phytophagous mites, cattle ticks and certain lepidopterous insects. Because of its unique spectrum of biological activity with regard to selectivity, chlordimeform may be the forerunner of a new class of agricultural chemicals. Although its mechanism of action is unknown, Knowles and Roulston[1], studying the action of chlordimeform and related compounds on the southern cattle tick, suggested that inhibition of monoamine oxidase (MAO) could be involved. This hypothesis was based on observations of ticks poisoned with formamidine compounds and on the known ability of amidine compounds, such as propamidine and pentamidine, to inhibit MAO from mammals[2]. We have observed that symptoms manifested by rats poisoned by chlordimeform and demethyl-chlordimeform are similar to those elicited by sympathomimetic agents including known MAO inhibitors (unpublished results of F. R. Johannsen and C. O. K.). Thus, it seemed appropriate to examine chlordimeform and related compounds as potential inhibitors of rat liver MAO *in vitro*.

For preparation of the enzyme, freshly dissected rat liver was rinsed with Ringer solution, and a 20% homogenate was prepared in distilled water, filtered through cheesecloth and centrifuged at 500g for 10 min. The supernatant was used as the MAO source. For MAO assay a standard incubation mixture contained 0.2 ml. of the enzyme preparation, 0.3 µmol of kynuramine, and 2.8 ml. of 0.05 M phosphate buffer, pH 7.4. Deamination of kynuramine was followed by a decrease in absorbency at 360 nm at 27° C as described by Weissbach et al.[3]. The inhibitory potency of chlordimeform and related compounds was examined by adding solutions of these compounds at various concentrations to the enzyme 30 min before addition of the substrate followed by the usual assay. All experiments were repeated at least twice, and the data were averaged. Data are expressed as I_{50} values which represent the concentration of the compound in mol/l. giving 50% inhibition of MAO activity.

The results of inhibition of MAO activity from rat liver by chlordimeform and related compounds are given in Table 1. When compared with iproniazid and tranylcypromine, two classical MAO inhibitors, chlordimeform (I) was a moderately strong inhibitor. However, demethylchlordimeform (II), a chlordimeform metabolite previously isolated from mammals,

insects, spider mites[4], and southern cattle ticks (unpublished results of C. A. Schuntner and C. O. K.), was even more potent than chlordimeform. This is especially interesting in view of the suggestion[1] that demethylchlordimeform is probably the actual toxicant in chlordimeform-poisoned southern cattle

Table 1 Inhibition of Rat Liver Monoamine Oxidase Activity by Chlordimeform and Related Compounds

Compound	Structure	$I_{50}(M)$
(I) Chlordimeform		1.4×10^{-5}
(II) Demethylchlordimeform		4.7×10^{-6}
(III) HOKKO-20013		1.1×10^{-5}
(IV) C-10405		2.2×10^{-5}
(V) BTS-27271		2.7×10^{-5}
(VI) C-17294		5.9×10^{-4}
(VII) C-17296		5.0×10^{-4}
(VIII) C-14640		7.2×10^{-4}
(IX) U-36059		6.6×10^{-7}
(X) Iproniazid		6.3×10^{-6}
(XI) Tranylcypromine		5.8×10^{-7}

ticks. Table 1 suggests that in the substituted aryl alkylforma-midines examined maximum inhibitory potency was associated with those compounds containing the 4-chloro-o-tolyl moiety. Thus, compounds I, II and III were more active MAO inhibitors than were compounds IV, V, VI, VII and VIII. U-36059 (IX),

an acaricide structurally related to the formamidines, was the most potent compound tested; its anti-MAO activity compared favourably with that of tranylcypromine.

We have shown that chlordimeform and several related compounds are potent inhibitors of the deamination of kynuramine by rat liver MAO *in vitro*. Although it is possible that these compounds will also interfere with other enzyme systems, it seems plausible to suggest that a causal relationship exists between the toxic action of these formamidine compounds and interference with the MAO-biogenic amine system. This is the first observation of inhibition of MAO by insecticides and acaricides.

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How Much Food Does Man Require?

WE believe that the energy requirements of man and his balance of intake and expenditure are not known. Paradoxically, we conclude this from results of the increasingly sophisticated studies of food intake and energy expenditure which show that in any group of twenty or more subjects, with similar attributes and activities, food intake can vary as much as two-fold[1-5]. In those surveys where both intake and expenditure are measured, there is often good agreement between the two estimates for the average of the group, but usually very large discrepancies between individual intake and individual expenditure. The results of careful studies in a number of countries suggest that some people, perhaps through some mechanism of adaptation, are able to be healthy and active on energy intakes which, by current standards, would be regarded as inadequate. On the other hand, there are also studies in which subjects have been given large quantities of additional food with little or no increase in body weight[6,7]. In contrast, there are the difficulties experienced by the obese in reducing body weight in spite of a drastic reduction of food intake, and the well recognized fact that many fat people eat no more, and sometimes less, than those who are not obese. These observations underline the extent of our ignorance about the mechanisms by which energy balance is maintained.

When the energy requirements of large populations are calculated, using the currently available international standards prepared by the Food and Agriculture Organisation and the World Health Organisation, then it may be, and often is, concluded that a large proportion of the world's population is undernourished; present standards put this proportion at about 70%. This estimate is based on a careful examination of all available information; such estimates are essential for governmental planning of, for example, food production. Some of us have assisted in this preparation and suggest these estimates with all their faults are the best that can be achieved on present knowledge.

It is possible, however, that the 30% of the world's population who have an "adequate" intake are really eating too much and that an unknown proportion of the rest are not undernourished. Our present information does not provide a satisfactory basis for more accurate estimates, as the methods commonly used are not precise enough and cannot be validated. Furthermore, the measurement of normal daily food intake and energy expenditure poses many technical and logistic problems, requires large teams of skilled staff and is expensive; hence so far only small populations of individual men and women have been studied. It is difficult to finance such work, and there are relatively few surveys in which individual food intake has been measured with acceptable levels of accuracy.

These are some of the reasons that prompt us to assert that we do not know how much food man requires. If there is merit in this assertion, and no doubt many will question it, we would stress that to determine man's energy need with more precision should be regarded as a major and urgent task. We believe that appropriate methods can be developed; for example, if a calorimeter suitable for man was available it would be possible to calibrate the various ways by which food intake, energy expenditure and energy balance are assessed. Calorimeters for domestic animals have been constructed, but none suitable for man exists today. This work would not be easy or cheap, but we suggest the social and political advantages of obtaining accurate answers could be immense.

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BOOK REVIEWS

Vive la Différence

Gender Differences: Their Ontogeny and Significance. Edited by C. Ounsted and David C. Taylor. Pp. x+273. (Churchill Livingstone: Edinburgh and London, 1972.) £4.50.

A Scottish medical professor once remarked that it was a pity there were not more women doctors; they are, he said, better people than the men. It was easy to discern his meaning, difficult to imagine a way of expressing it objectively. Most of this useful book is at the other extreme: it gives, systematically, the hard facts about the subtler differences between the sexes. The contents of most chapters (and the drab production) suggest that something like a textbook was aimed at.

C. O. Carter gives a helpful, if apparently hurriedly written, review of sex-influence ("sex-limitation") and sex-linkage. His account of the interaction of genotype and environment in the aetiology of pyloric stenosis is especially instructive. P. E. Polani puts the reader up-to-date on sex-chromosome anomalies. I. N. Mensh and John Bancroft contribute overlapping chapters on the role of the social environment in the determination of "gender identity"—that is, what sex one feels oneself to be. That of Mensh, which consists largely of quotations from the work of R. J. Stoller and his colleagues, is particularly interesting. It begins with the selected young men of Madagascar, Tahiti and other regions who were raised as girls and considered themselves completely feminine; it ends with a pessimistic discussion of the prognosis for treatment of trans-sexualism; in between there is some notable evidence of the phobias from which many (American) physicians suffer in dealing with these "disorders".

Corinne Hutt provides a long, wideranging review with much valuable documentation on effects of separation from the mother, other aspects of social behaviour, and the development of intellectual abilities. There is a strenuous effort to be critical; but comparisons between men and women, like those between races and social classes, are technically as well as politi-

cally hazardous. For example, Dr Hutt does not consistently distinguish between saying that women are different from men and saying that they are superior or inferior. The importance of this emerges in a report by Hugh Fairweather and John Hutt, on studies of reaction time at various ages. Is it better to have a short reaction time or a long one? Presumably, for a given task, there is an optimum; and the useful thing to know is the distributions of scores about this figure.

Detailed analysis of sex differences leads to few simple conclusions. A. W. H. Buffery and J. H. Gray examine the ontogeny of spatial and linguistic skills. Girls and women usually score lower than boys and men in manipulation of spatial relationships, but not in other visual tasks. Girls are notoriously more fluent speakers than boys, yet are often found to have smaller vocabularies. But these statements about averages say nothing on the distributions of the scores; and the existence of a big overlap between distributions may be more important than the differences between the means. There are other complications: in one enquiry on the perception of space, female scores were unimodal, but the male scores were bimodal.

Often, indeed, differences between means, even if enormously "significant" statistically, are of trifling value for practical purposes. Christopher Ounsted and David Taylor devote an important but not entirely lucid chapter mainly to the clinical implications, actual or hypothetical, of the well-known fact that populations of men tend to vary more than those of women. Hence we have the superiority of men over women in the production of idiots. They discuss the incidence, in relation to age and sex, of a number of neurological disorders, infectious illnesses and other diseases; and they attempt an interpretation of the figures in terms of the increased variance imposed by the presence of a *Y*-chromosome. Their chapter is appropriately preceded by two of a less speculative character. Margaret Ounsted reviews intra-uterine growth.

And Martin Vessey writes on gender differences in the epidemiology of non-neurological disease; this chapter is an admirably lucid account of carcinoma of the lung, carcinoma of the stomach and ischaemic heart disease. The incidence of these conditions in relation to sex and age presents a fascinating, if sometimes dismaying, picture.

Knowledge in this field is growing quickly, and I hope the editors will be willing to organize a second edition after a few years. If so, the methodology could be tightened up. This applies especially to the uses of analogies with other species; and, still more, to the treatment of the interaction between heredity and environment, over which several contributors stumble. Dr Carter, instead of ending his chapter abruptly, could have helped both his colleagues and his readers by concluding with a clear explanation of how to make valid statements on this subject. Minor needs include a summary for every chapter, an author index, and uniform treatment of tabular material: statements of means should always be accompanied by the number of observations in each class and a measure of the variance: all measures should be in metric; and abbreviations should conform to international standards.

This book may not tell us whether women are "better people" than men, but it gives the type of authentic information on which the decisions of governments, teachers, doctors and others should be based.

S. A. Barnett

Future of Rubber

Natural Rubber and the Synthetics. By P. W. Allen. Pp. 255. (Crosby Lockwood: London, December 1972.) £4.95.

This book is essentially the history of the fight of natural rubber to retain its position as a major rubber in competition with the synthetics. It contains a broad analysis of the structures of the two very different indus-

tries, together with a technical comparison of the behaviour of both natural and synthetic products in the modern rubber manufacturing industry.

Although the author, in spite of his natural rubber bias, expects that natural rubber will increasingly be replaced by synthetics where price makes them competitive, he can find no evidence to suggest that the production of natural rubber will decline in absolute terms. Indeed, natural rubber is still the preferred polymer for many high performance applications (for example, truck tyre carcasses) and even in the short term there is a relatively untapped potential for technological improvement which results from the late application of science-based research in this industry. Indeed, on the basis of the evidence presented in this book, the synthetic rubber industry has had a beneficial stimulatory effect on the natural rubber industry. The latter has belatedly learned the need for effective technical specification and efficient presentation of its product.

In the long term, too, natural rubber probably has the greatest potential for cost reduction. Effective steps have already been taken to improve the profitability of natural rubber by the selection of high yielding clones and by the development in recent years of yield stimulants. At the same time that the synthetic rubber industry is faced with the prospect of higher raw materials costs, the yield improvement in natural rubber has tipped the economic scales slightly in favour of the natural product.

This book is written in a style which is easy to read and it does not assume specialized technological or economic knowledge. Perhaps the most interesting chapters are those concerned with the economic structures of the two industries. These do, however, suffer from the deficiency that hard facts are not always available. Nevertheless, the book is a valuable starting point for students of technological economics who are concerned with the future of the rubber industries.

GERALD SCOTT

Quantum Field Maths

Mathematics of Contemporary Physics. Edited by R. F. Streater. Pp. xi+274. (Academic: New York and London, December 1972.) £6; $17.50.

ONE important theoretical problem in high energy physics today is to obtain a better understanding of quantum field theory. Many models claiming to be good descriptions of the properties of elementary particles are still languishing for want of powerful enough field theoretic techniques to calculate their detailed predictions. Because of this pressure there is a great

deal of activity at present attempting to lay a firm mathematical foundation to quantized systems with infinitely many degrees of freedom.

The volume under review comprises the contents of the major lectures given at an instructional conference at Bedford College in September 1971 on this theme. As such, the title is misleading, for there are many areas of mathematics of contemporary physics other than those reported on. As a collected set of lectures in the more select area of Hilbert spaces, operators thereon and operator algebras, and their applications to problems of quantum field theory and quantum statistical mechanics, the volume is a very valuable contribution to those who wish to enter this field or even to find out in general what success is being achieved.

The lectures open with a useful introduction by R. Haag to the basic ideas of quantum field theory, and continue with a very valuable and reasonably self-contained course by B. Simon on functional analysis of operators on a Hilbert space and related topics. There is then a detailed discussion from J. Glimm and A. Jaffe of the existence problem for boson quantum field models, the basic properties of two or three dimensional self-interacting models being discussed, including how to deal with infinite counter-terms. There is then a description of the axiomatic approach to statistical mechanics by N. Hugenholtz, a brief guide to the rigorous theory of quantum scattering by K. Hepp, a presentation of Segal's theory of linear fields by P. Bongaarts, an analysis of the free boson gas by J. Lewis and of the Lorentz transformation properties of self-interacting boson fields by A. Klein. The volume concludes with a course of algebras with quasilocal structure and factorizable representations.

The majority of the courses are at a high level, and would undoubtedly be difficult for the casual reader. For the research worker, be he mathematician or theoretical physicist, who wants to perform research in quantum field theory or in operator algebras with relevance to physics, this volume allows him to come to grips with the most valuable recent work in the field. As such it will be indispensable for the second year research student; it should also prove valuable to the more advanced research worker.

The only defect of the book is that there is little general discussion of progress, of whether the problem posed by a realistic quantum field theory, such as that of electrodynamics, is being approached. But then it may be up to the readers of the book to make the contributions which will achieve that. Undoubtedly there is much yet to be done in this area. J. G. TAYLOR

Drug Dependence

Chemical and Biological Aspects of Drug Dependence. Edited by S. J. Mule and Henry Brill. Pp. 561. (The Chemical Rubber Company: Cleveland, Ohio, 1972.)

MANY drugs exist which have little in common except their ability to produce dependence—the word now favoured throughout the world for addiction—which because of its moral connotations inhibits rational and scientific investigation of the social and medical problems which arise from the ability of such drugs to affect mental processes. Nevertheless, it is the existence of these problems that has led to the upsurge in concern about the chemical and biological properties of the psychoactive substances amongst which are some of the oldest and newest of the drugs known to man. The present volume is a comprehensive compendium of information about drugs currently known to produce dependence in man or animals. It is written in the form of a series of twenty-five authoritative and virtually self-contained reviews loosely grouped together. References to the literature are copious but not exhaustive and in the main are to literature that has appeared within the past five years up to and including 1971.

The five sub-sections into which the book is divided deal with the social and medical significance and biological characteristics of drug dependence; criteria for its evaluation; the chemistry of the drugs involved; their physiological and pharmacological properties and, finally, the biochemical, metabolic and endocrinological consequences of their use and abuse.

Perhaps inevitably there is considerable overlap between chapters and information about individual drugs is scattered diffusely throughout the volume, which makes the absence of an index the more lamentable. What might be considered the forensic and clinical aspects of drug dependence are rigorously excluded. Surprisingly, this detracts comparatively little from this book, which fills an important gap in our knowledge. Nevertheless, it robs the otherwise excellent chapter on the detection and identification of drugs of dependence of any discussion of the usefulness, or otherwise, of the enormous number of urinalyses currently undertaken in clinical laboratories in this country and elsewhere.

The aim of the publishers to provide "highly authoritative reference works dealing with those subjects for which there exists an urgent necessity for published information . . ." has undoubtedly been fulfilled. Such aims do not lend themselves well to the development of literary style, but for anyone concerned with the problems

of drug dependence, however remotely, this book will prove invaluable as one that brings together information otherwise only to be found scattered throughout the literature of many unrelated academic disciplines.

VINCENT MARKS

Mass Spectrometry

Principles of Organic Mass Spectrometry. By Dudley H. Williams and Ian Howe. Pp. 245. (McGraw-Hill: London and New York, November 1972.) £5.

THIS is a useful, indeed a very valuable, little book which outlines most of the aspects of modern mass spectrometry currently being investigated and presumably represents a fairly elementary series of university lectures. It comprises a series of comprehensive if rather condensed chapters upon the mass spectrometer, ionization and energy transfer, metastable ions, the quasi-equilibrium theory, energetics of ion decomposition, the relationship between fragmentation pattern and structure, isotopic labelling, collision processes, field ionization, ion structures, gas chromatography–mass spectrometry and the use of the computer in mass spectrometry. Each chapter concludes with a succinct list of relevant reviews and cognate papers useful for further reading. The book concludes with a useful index.

There are some trivial points raised in the text, and the few following items invite more serious criticism. Firstly, the attention paid to S.I. units is uneven, suggesting that one author may be less than enthusiastic about this new innovation. It may have been desirable to have included a table equating the newer units with the traditional ones of torr, kilocalories and so on. The second is the needless confusion occasioned in the mind of a beginner in this field by failing to call attention to the difference between H when the magnet is held steady while the voltage varies, and B—the magnetic induction—when the magnetic field is varying (page 4, 1's 1 and 2) rather than the voltage. This book also commits the now standard error of misquoting Stevenson's Rule (pages 94–97).

A further source of regret is occasioned by the practice of including valuable if not vital information in the form of footnotes or commentaries upon the tables. Much of the material so conveyed is often vital to a logically presented argument which, therefore, loses something of its power.

This book is well produced and is in the best traditions of scholarship. It is printed in a very clear legible type and is accompanied with a set of excellent explanatory diagrams. Both the publishers and the authors are to be

congratulated upon the production of this book. ROWLAND I. REED

Fossil Manual

Palaeontology and Geological Time. Prepared by the Course Team. (The Open University. Science: A Second Level Course.) Pp. 64. (The Open University: Bletchley, Buckinghamshire, 1972.) £1.10.

AUTHORS of this type of remote-control laboratory manual carry an enormous responsibility to their followers because they will have limited opportunity to rectify misunderstandings and textual errors. Thus, though one would wish to welcome such a venture in principle, one cannot help being disappointed at the outcome. This is a pity: a great opportunity has been missed for raising standards of geology teaching in many secondary schools and first-year university classes. Instead, an attractively designed, seemingly cheap, 63-page booklet has appeared on the market, which will doubtless sell well as a pre-examination crib despite the following glaring deficiencies.

The adult user will be deprived of basic facts necessary to comprehending the study as a result of over-simplification. The younger user, or by-product, on the other hand, will have absorbed a doctrinaire approach which, when based on misleading statements, will undermine his receptiveness for subsequent professional training. Thus, for all its good points in bringing science to the man in the street, this volume sets a dangerous educational precedent; when it could so easily have contributed substantially to an advancement of the science at no extra cost.

The text is arranged in a series of introductory paragraphs copiously illustrated with classical diagrams, which are followed by outline quizzes reminiscent of a weekly woman's magazine. The desired answers to these self-assessment tests are at the back of the book, but unfortunately they do not explain the reasons for eliminating alternative answers (for example, SAQ3 *c* and *f*). Thus, those who have erred, and even may have been technically correct, remain lost.

The best aspects of the volume are its glossary and its attempt to cover the broad field of palaeontology. The weaknesses lie in its keys, particularly Table 2, which is biologically misleading; elementary scientifico-grammatical inaccuracies in technical diagrams (SAQ4B6; SAQ6D4; SAQ9F7); clumsy annotations, bar scales are never used to indicate sizes; naïve popularizations of complex themes, for example, coral clocks and intraspecific variation. The unfortunate adoption of North American examples, where European alternatives are available, is surprising.

But the worst aspect of all is the treatment of the "Fossilization Process", which is wholly inadequate.

This is a neo-classical exercise book, complete with errors. In failing to delimit the limitations of their keys the authors show little appreciation of the biological and consequent mineralogical background of palaeontology; thus the consequences reveal themselves as a shower of random facts. Thus the volume is best suited to redeploying the energies of 12-year-old boys and their fathers on wet holidays.

J. A. E. B. HUBBARD

Parapsychology

Psychical Phenomena and the Physical World. By Charles McCreery. Pp. 158. (Hamish Hamilton: London, January 1973.) £2.30.

MR MCCREERY'S book, written with clarity and objectivity, is the fourth volume of the Proceedings of the Institute of Psychophysical Research, and continues the study of lucid dreams (those in which the subject knows he is dreaming), ecsomatic experiences and the philosophical and scientific questions raised by these and considered in earlier proceedings. The book is divided into a first part dealing with philosophical questions raised by such experiences, and a second containing empirical material.

The former considers lucid dreams, ecsomatic experiences, apparitions, materializations and psychokinesis. It discusses such questions as the criteria whereby we may distinguish the waking from the sleeping state; perception in out-of-the-body experiences and the difficulty of distinguishing between physically seeing the world and having hallucinatory perceptions which correspond to it; the problem of establishing complete satisfactory standards of distinction between apparitions and "real" people; the nature of materialization, and the differences between materialization, apparitions and physical objects; and the fact that, though psychokinesis seems inconceivable, yet we cannot explain how we move objects physically, nor do we even know how we control our limbs.

The empirical section of the book begins with an account and analysis of a number of extra-sensory perception card-guessing tests, investigating the capabilities of eldest, only and younger children in family order. In the three most significant experiments eldest children did best, although other factors such as their socio-economic groupings affected the results. There follow studies of a lucid dreamer, the Marquis d'Hervey de Saint-Denys, born 1822, who published a detailed record of his dreams; the lucid dreams and ecsomatic experiences of "Subject E"; and some

miscellaneous cases of ecsomatic experiences containing common features such as the feeling of being "above" the physical body, autoscopy (the seeing of one's own body), the subject's emotional relationship to his physical body in the ecsomatic state, and the seeing of things, sometimes by "travelling", which subjects could not see in their physical bodies. The work ends with an account of experimental evidence of the fulfilment of a previous prediction of the author that subjects whose alpha-frequency was accelerated above their own pre-test baseline in electroencephalogram recordings did better in ESP tests than others.

The value of the book lies in its accumulation of case-material and the raising of questions suggested by this. Scientists, theologians, parapsychologists and psychical researchers will find it useful and stimulating.

D. CHRISTIE-MURRAY

Story of Immunology

The Science of Self: a Report on the New Immunology. By David Wilson. Pp. xii+346. (Longman: London, June 1972.) £2.75.

THIS exemplary text on "the new immunology" is good enough to be read as a primer by beginners in the field—by PhD starters, for example, by surgeons turning their hand to immunological research, or by anyone whether in the health business or not anxious to get a synoptic view of the most exciting branch in modern medical biology.

For Wilson the new immunology grows out of the study of self-recognition. The special virtue of this approach is that it makes it possible to embrace cancer immunity and auto-immunity within one comprehensive narrative. From the standpoint of the history of ideas the most interesting thing about immunology is how little progress it made between the great days of Behring, Bordet and Koch, and its modern developments by chemists, zoologists, molecular biologists and experimental surgeons. The reason is that over the whole of the period during which it was in the doldrums immunology was running along what may be called "Rothschild" lines, that is, orientated strictly towards practical usefulness and material advantage—antisera, vaccines and the like—without sufficient attention to chemical and biological fundamentals. In this conception of the way science ought to develop the kind of skin-grafting work that played such a large part in the growth of the new immunology might easily have been dismissed as laboratory play.

The New Immunology is a very good story and David Wilson has both the

technical knowledge and the literary skill to make it clear that it is so.

P. B. MEDAWAR

Harvesting the Waters

Aquaculture: The Farming and Husbandry of Freshwater and Marine Organisms. By John E. Bardach, John H. Ryther and William O. McLarney. Pp. xii+868. (Wiley: New York and London, November 1972.) £15.95.

THIS is an ambitious book devoted to a subject which is attracting increasing attention. Most of the important natural resources of fish and shellfish in the sea have now been discovered and exploited, and in areas such as the North Atlantic the amount of fishing effort deployed is already more than enough to harvest the maximum sustainable yield in an economic manner. On the land, development and pollution may seriously restrict freshwater fish production, while in the intervening estuaries and coastal fringes conditions have often sadly deteriorated as the result of industrialization. In such circumstances the possibilities of land-based culture systems for fish, molluscs and crustaceans, and of "farming" shallow coastal waters, are beginning to look increasingly attractive. Thus the book is very timely, particularly because of its very wide coverage. It is also very clearly written in plain English and well illustrated by clear photographs and line diagrams.

The plan of the book is straightforward. The first chapter establishes general principles and examines the economics of different culture systems. It is followed by no less than forty-two specialized chapters dealing successively, among many others, with carp, catfish, mullets, milkfish, *Tilapia*, eels, salmonids, sturgeon, pompano, yellowtail, marine flatfishes, shrimps, lobsters, freshwater crayfish, oysters, mussels and seaweeds. There is a useful appendix on pond siting and construction.

References are given separately after each chapter; the coverage varies, but is sometimes rather less than one might expect—eighteen references to the culture of freshwater salmonids seems a meagre guide to anyone wishing to consult the original papers. There is, moreover, no chapter on Atlantic salmon, although its Pacific cousins receive separate treatment in a very informative chapter of fifty-one pages.

In addition to references, the authors give after each chapter a list (with addresses) of those people interviewed or from whom they received personal communications. There are some unexpected gaps; to a European, for example, it is strange to find no Dutch references in the chapters on oyster and mussel culture. On the other hand,

the book is particularly informative about Japanese and Far Eastern practices which are not well described in easily accessible references. Another good feature is its insistence on looking realistically at the economic prospects of the culture systems described. All in all, this is a very useful book although, despite its length, the specialist must still seek out the original papers and must not assume that coverage is complete. He will, however, usually find some stimulating ideas.

H. A. COLE

Plant Viruses

Principles and Techniques in Plant Virology. Edited by Clarence I. Kado and Hari O. Agrawal. Pp. xv+688. (Van Nostrand Reinhold Company: New York and London, 1972.) £14.10.

THIS is a very useful book indeed, even though it can hardly be expected to fulfil the claim on the dust cover to include "in extensive detail both the principles and techniques of every aspect of plant virology". Besides control measures and nomenclature (which were omitted for stated reasons not necessarily valid) insect vectors other than aphids and leafhoppers, for example, are not considered.

The book will be helpful to research workers seeking information on recently developed techniques. These develop very rapidly, however, and I was not surprised to find a few places where information was already incomplete. For university lecturers and their students this book will fill a long-felt need.

It is divided into four parts. The first, which is called "Biology of Plant Viruses", comprises chapters on inoculation principles, inhibition, interference and acquired resistance, inclusion bodies, and (oddly placed) electron microscopy. The second deals with transmission by aphids, plant hoppers, mites, nematodes, and fungi, and through seed and pollen. The third part on "Isolation and Characterization" contains chapters on purification, preparative centrifugation, chromatographic purification, electrophoresis, isolation and properties of virus proteins, virus degradation and nucleic acid isolation, serology and analytical ultracentrifugation. The fourth part, called "Photobiology and Mutation", is more esoteric and less concerned with methodology.

Each chapter is authoritative, having been written by a research worker specializing in the subject, and reflects the outlook of the author. The standard of clarity, if not uniform, is certainly high. The editors must be congratulated on compiling a book which should be on hand for reference in all plant virus laboratories.

A. F. POSNETTE

CORRESPONDENCE

Dingle's Question

SIR,—Professor J. Ziman[1] and Mr G. F. R. Ellis[2] seem not to have read my "question", let alone answered it, though Ziman quotes it correctly. Neither of the events need be at either of the clocks concerned, so the statement, "the fastest working clock between any two events is one that travels between them by free fall", is futile.

Two observers-cum-clocks, A and B, are in uniform rectilinear relative motion. Each receives light from each of the same two events, occurring at any ascertainable positions at any times, and, *using the theory*, finds the times by his clock at which the events occurred. These times will be separated by intervals, dt for one clock and dt' for the other, and these intervals, *according to the theory*, will be related by the Lorentz transformation, and so will be unequal. My question is: how does the theory indicate which clock gives the larger interval? If A has velocity O and B velocity v, the Lorentz transformation makes that clock A; if B has velocity Õ and A velocity v, it makes that clock B. Also, *according to the theory*, these assignments of velocity are equally valid. Hence, unless my question receives an acceptable answer, the theory requires each clock to give a larger interval between the same events (i.e. to work faster) than the other, which is impossible.

It is not a case of each clock appearing to work the more slowly to an observer with the other. A and B observe only the events, not each other, and each may be ignorant of the other's existence. They can be brought together later, introduced, and asked to compare notes. What feature of the situation enables us to say, consistently with the theory, which set of clock-readings has yielded the larger interval between the events? Is there no one who will answer that question, or have the courage to admit the obvious fact that no answer is possible and therefore the theory must be false?

Yours faithfully,
HERBERT DINGLE

Purley,
Surrey

[1] Ziman, J., *Nature*, **241**, 143 (1973).
[2] Ellis, G. F. R., *Nature*, **242**, 143 (1973).

Obituary

Academician K. I. Skryabin

ACADEMICIAN KONSTÁNTIN IVANOVICH SKRYABIN, one of the leading Soviet specialists in the medical and veterinary sciences and virtually the founder of helminthological research in the Soviet Union, died on October 17, 1972, at the age of 93.

Skryabin was born on December 7, 1878, in St Petersburg. His father was a railway engineer, and his international family background gave the young Skryabin an unusually wide outlook on life.

After an unsettled early education Skryabin enrolled in the Yur'ev (now Tartu) Veterinary Institute in 1900. Here his work quickly attracted the attention of the Director of the Institute, Professor K. K. Raupakh, who in 1903 took Skryabin as one of a small party of specially privileged students allowed to attend the First All-Russian Veterinary Congress held in St Petersburg.

In 1905 he graduated from the Yur'ev Institute, and began his career as a veterinarian working in Central Asia. In 1912–14 he made a prolonged visit to western Europe, working at Königsberg and Neuchatel Universities and the Alfort Veterinary School.

On his return to Russia he was appointed Head of Department of Veterinary Medicine and Zoohygiene of the Statbutov Higher Agricultural Courses for Women (the equivalent of university courses for women at that time).

In 1917, he became Professor of Parasitology at the Don Veterinary Institute, in Novocherkassk, and thus was able to begin his intensive work on helminthology, a subject which had first attracted his attention during his time in Central Asia. In 1920 he became Head of the Helminthology Department of the All-Union Institute of Experimental Veterinary Medicine and Head of the Department of Parasitology of the Moscow Veterinary Institute, and from then onward held a number of high academic and teaching posts, culminating in his appointment in 1956 as Vice-President of the All-Union Lenin Academy of Agricultural Sciences, a position which he held until 1971. He became an Academician of the Soviet Academy of Sciences in 1944, and was subsequently elected an honorary member of the Academies of Bulgaria, Hungary, Czechoslovakia, East Germany, Yugoslavia, France, and of Scientific Societies in the USA, Great Britain, Belgium, West Germany and India.

Skryabin published more than 700 papers and monographs on various aspects of helminthology and parasitology including: *K kharakteristike gel'mintofauny domashnikh zhivotnykh Turkestana* (on the characteristics of the helminthofauna of domestic animals of Turkestan—1916; his doctoral thesis); *Askaridy i ikh znachenie v meditsine i veterinarii* (Ascarides and their significance in medicine and veterinary science—1925); *Trematody zhivotnykh i cheloveka* (Trematodae of animals and man, 20 volumes, 1947–62), *Osnovy nematologii* (Principles of nematology, 10 volumes, 1949–61), and his autobiography *Moya zhizn' v nauke* (My life in science—1969).

Skryabin devoted great efforts to developing the study of helminthology throughout the Soviet Union, founding helminthology departments in scientific institutions and universities in almost every republic of the USSR. In the early 1920s he also founded the three major helminthological bodies in the Soviet Union: the Helminthological Department of the State Institute of Experimental Veterinary Science (later transformed into the All-Union Institute of Helminthology, which bears his name), the Helminthology Department of the Moscow Tropical Institute, and the Helminthology Bureau of Moscow State University, which in 1942 became the Helminthology Laboratory of the Soviet Academy of Sciences, and of which Skryabin remained the head until his death.

He was extremely interested in promoting international cooperation in helminthological research, and it was on his initiative that commissions for

international research and practical work within the framework of the COMECON block were set up and the international journal *Gel'mintologiya* (Helminthology) was founded. He was also a co-editor of a number of Soviet publications on veterinary medicine and a member of the Editorial Board of *Meditsinskaya parazitologiya i parazitarnye bolezni* (Medical parasitology and parasitic diseases).

Skryabin took part in numerous All-Union and International Congresses on Helminthology. He also led more than 300 helminthological expeditions to all parts of the USSR. For his work, which won him in his lifetime the unofficial title of "Founder of Soviet Helminthology", his official recognitions include the Order of Lenin (6 times), the Order of the Red Banner of Labour (3 times), the Order of the Red Star, two Stalin Prizes (1941 and 1950), a Lenin Prize (1957), and numerous medals, scrolls of honour and other decorations.

Announcements

Appointments

Dr. R. G. Priest, St. George's Hospital Medical School, has been appointed to the Chair of Psychiatry, at St. Mary's Hospital Medical School.

Dr. R. R. Trussell, Department of Health and Social Security, has been appointed to the Chair of Obstetrics and Gynaecology at St George's Hospital Medical School.

Miscellaneous

David William Greene, Dublin Institute of Advanced Studies, has been elected President of the Royal Irish Academy, as from March 1973.

Corrigendum

In the article What Cooks with Solar Neutrinos? by William A. Fowler (*Nature*, **238**, 24; 1972), the first part of the second paragraph under "Experimental Physics" should read: "In some rudimentary calculations I have assigned optimum properties to this proposed resonance. The resonant energy, $E_r = 20$ keV, and the width, $\Gamma_r = 10$ eV, were chosen to match the most effective energy and to be less than the effective interval (10 keV) in energy for $^3\text{He} + ^3\text{He}$ in the Sun, respectively. The narrow width chosen also guarantees that the resonance is not detectable at the lowest energies of measurement on $^3\text{He}(^3\text{He},2p)^4\text{He}$. The spin and parity were taken to be O^+ so that an $l = 0$ interaction was possible and the dimensionless reduced width in the incoming channel was taken to be unity, yielding $\Gamma(^3\text{He} + ^3\text{He}) \approx 10^{-6}$ eV at resonance. The reaction rate from the resonance is $\sim 10^4$ times that extrapolated without resonance from the low energy measurements[7]. This result is approximately independent of the choice of Γ_r as long as it is small compared to 10 keV." I am grateful to Dr M. R. Dwarakanath for pointing out the necessity for this correction.

Reports and Publications

not included in the Monthly Books Supplement

Great Britain and Ireland

Forestry Commission. Guide Map to Your Forests. (London: Publications Officer, Forestry Commission, 1973.) 30p. [291

Agricultural Research Council. Poultry Research Centre—Summary of Research Reports published in the year ending 31 March, 1971. Pp. viii+56. 35p net. Poultry Research Centre—Summary of Research Reports published in the year ending 31 March, 1972. Pp. xiii+82. 50p net. (London: Agricultural Research Council, 1972. Obtainable from HMSO.) [291

Universities Research Reactor. Annual Report, 1971/1972. Pp. v+37. (Risley, Warrington: Universities Research Reactor, 1973.) [291

Scholarships Guide for Commonwealth Postgraduate Students, 1973/1975. Pp. 252. (London: The Association of Commonwealth Universities, 1972.) 65p. [301

The BBC in the Eighties: The Relationship Between Broadcasting Policy, Programme Needs and Technological Potential. By Charles Curran. (Speech given to the Institution of Electrical Engineers, 14 November, 1972.) Pp. 22. (London: BBC, 1973.) [301

The Proper Priorities of Science and Technology. By Professor Dennis Gabor. (The Eighteenth Fawley Foundation Lecture.) Pp. 16. (Southampton: The University, 1972.) 20p. [311

Bulletin of the British Museum (Natural History). Geology. Vol. 21, No. 2: Postcanine Occlusion in Cynodonts and Tritylodontids. By A. W. Crompton. Pp. 27–71+7 plates. £3.40. Zoology. Vol. 24, No. 1: The Genus *Euaugaptilis* (Crustacea, Copepoda). New Descriptions and a Review of the Genus in Relation to *Augaptilus, Haloptilus* and *Pseudaugaptilus*. By J. B. L. Matthews. Pp. 1–71. £2.85. (London: British Museum (Natural History), 1972.) [311

National Institute of Industrial Psychology. Annual Report and Statement of Accounts for the year ended 30 September 1972. Pp. 39. (London: National Institute of Industrial Psychology, 14 Welbeck Street, W1, 1973.) [311

Other Countries

Smithsonian Contributions to Zoology. No. 134: Additions to Revisions of the Blenniid Fish Genera *Ecsenius* and *Entomacrodus*, with Descriptions of Three New Species of *Ecsenius*. By Victor G. Springer. Pp. iii+13. (Washington, DC: Smithsonian Institution Press, 1972. For sale by US Government Printing Office.) 30 cents. [181

Sudan. Agricultural Research Corporation. Technical Bulletin No. 3 (New Series): Leaf Curl of Tomato. By A. M. Yassin and H. S. Abu Salih. Pp. 24. (Hudeiba: Botany and Plant Pathology Section, The Research Station, Agricultural Research Corporation, 1972.) [181

US Department of the Interior: Geological Survey. Bulletin 1314-F: Trace-Element Contents of Some Plutonic Rocks of the Sierra Nevada Batholith. By F. C. W. Dodge. Pp. iii+13. 55 cents. Water-Supply Paper 1939-D: Chemical Quality of the Water in the Tucson Basin, Arizona. By R. L. Laney. Pp. iv+46+5 plates. Water-Supply Paper 2016: Quality of Surface Waters of the United States, 1967. Parts 12–16: North Pacific Slope Basins, Alaska, and Hawaii and other Pacific Areas. Pp. xvi+431. Professional Paper 562-J: Summary of Alluvial-Channel Data from Rio Grande Conveyance Channel, New Mexico, 1865–69. By J. K. Culbertson, C. H. Scott and J. P. Bennett. Pp. iii+49. 70 cents. Professional Paper 691: Stratigraphy and Origin of the Triassic Moenkopi Formation and Related Strata in the Colorado Plateau Region. By J. H. Stewart, F. G. Poole and R. F. Wilson. Pp. v+195+5 plates. Professional Paper 741: The Quinary Reciprocal Salt System Na, K, Mg, Ca/Cl, SO$_4$—a Review of the Literature with New Data. By J. J. Rowe, G. W. Morey and C. S. Zen. Pp. vi+37. 50 cents. Professional Paper 745: Geology and Uranium Deposits, Shirley Basin Area, Wyoming. By E. N. Harshamn. Pp. vii+82. Professional Paper 760: Paleomagnetism of some Lake Superior Keweenawan Rocks. By Kenneth G. Books. Pp. iv+42. 50 cents. (Washington, DC: Government Printing Office, 1972.) [181

Is the End of of the Strategic Balance in Sight ?

THERE are signs that the strategic doctrines by which the United States and the Soviet Union have kept each other at bay since the late 1950s are nearing their end. It is several months now since the doctrine of mutual deterrence was repeated in official language—a significant omission at a time when the Department of Defense in the United States is fighting to get its annual budget through Congress. The most suggestive straw in the wind, however, is the appointment of Dr Charles Ikle, now a sociologist with the Rand Corporation, as head of the United States Arms Control Agency. Dr Ikle is a distinguished academic, but, more significantly, is one of those who have been urging that the United States should try to define a military strategy different from the doctrine that potential enemies must be made to realise that military adventures are unthinkable—rashness would invite all-out retaliation and an entirely unacceptable level of damage. It is unlikely that any United States President, but President Nixon least of all, would agree to appoint a director of the United States Arms Control Agency if his views were unacceptable. So the question arises whether a departure from the doctrines of mutual deterrence is to be welcomed or feared.

First, however, it must be acknowledged that the US Arms Control Agency is no longer what it used to be. In 1961 it was intended as the chief workhorse of President Kennedy's determination that genuine measures of disarmament and arms control should be made to see the light of day. Its achievements have been considerable for the first few years of its existence. The agency, small though it may have been, turned out to be a powerful means of holding the ring between the familiar vested interests in the United States—chiefly the Department of Defense and the State Department, with organizations such as the Atomic Energy Commission looking on. Since the resignation of Mr C. C. Smith last year, however, the agency has been without a director and it has become plain that the agency was in for a hard time.

Dr Ikle's appointment does at least suggest that the agency will survive, which is something to be grateful for. Its shrunken budget also implies that the Administration is planning to concentrate some of the functions of the agency in the White House, where the ubiquitous Dr Henry Kissinger functions. And although nobody would dispute that Dr Kissinger would make an excellent director of the Arms Control Agency if he had the time, can the Administration be so sure of itself that it can now safely dispense with allies in one of the few good causes which has a chance of yielding benefits in the next few years?

The proposal that the doctrine of mutual deterrence should now be modified is intricate, and calls for wide debate. There are arguments on both sides, and nobody would pretend to know for sure how they should be weighed against each other. The present doctrines have their origin in the cold war of the 1950s and were the chief contribution of the United States. The argument then was that the capacity to threaten widespread destruc-tion of Soviet cities was the most practical—even the most economical—way of inhibiting even conventional military adventures. Over the years, the Soviet Union has equipped itself with the means of replying in kind. For much of the 1960s, the "balance of terror" was complete and convincing to both sides.

So why should there now be a change of strategy? It is fair to say that the Soviet Union has never been entirely convinced and has kept adding to its stock of conventional weapons, airborne and naval. No doubt the United States has also been dismayed that the existence of potentially overwhelming weapons has uncomfortably frozen situations in which conventional warfare might previously have been possible—Vietnam is an obvious example, but the invasion of Czechoslovakia in 1966 was a reminder of how the political situation in Europe has been frozen by the existence of nuclear weapons. But there is now no chance that a modification of the nuclear strategies will ever again make it appear simple to settle political differences by conventional wars—and most people will be glad of that. What has changed, however, is the accuracy of missiles. Mutual deterrence depends on one power's confidence in its capacity to retaliate being unharmed by the fear that its adversary might launch an unexpected attack. As things are, it is unlikely that enough is known of the exact positions of missile silos, and that the other side's weapons are sufficiently accurate for that to be an immediate possibility. That is at least one component of the argument in favour of a less rigid reliance on all-out retaliation.

Another incentive for the consideration now apparently being given to the changing of nuclear strategy is the possibility that familiarity with nuclear weapons may make the threat of all-out retaliation less credible than it has been in recent years. If, for example, it is possible in future for one super-power to destroy, say, half the other's missiles, the nation attacked might decide to negotiate, not retaliate. Or that is what the aggressor might calculate—a more alarming possibility. But a more varied strategic armoury would give both sides more options. To that extent a less complete reliance on mutual deterrence would be a benefit.

The most convincing case for a broadening of the strategic policies now followed by the Soviet Union and the United States is, however, the prospect that there may be in the next few years some further benefit from the long-drawn out SALT negotiations on the limitation of strategic weapons. There is even a possibility that the numbers of strategic weapons actually deployed may eventually be so markedly reduced that the threat of being able to inflict overwhelming damage on the other side may be reduced to the point of incredibility.

But there is a sense in which the credibility of the policies of the past few years has stemmed from the way in which the theory of mutual deterrence has been argued widely in professional circles and in public. If indeed there is now to be a change—and there is no

reason why present theories should be frozen indefinitely —it is imperative that these changes should also be argued in public. It may be anomalous that the head of a disarmament agency should be involved in the public justification of a new defence policy but that will have to be Dr Ikle's function. And, of course, it would be unreasonable to expect that any changes there may be could become apparent in the near future.

AID on the Increase

THE report of the panel on the use and practice of Artificial Insemination by Donor* which was set up by the British Medical Association's Board of Science in 1969 is to be welcomed. It is now thirteen years since Lord Feversham and his committee brought in their report on AID and a great deal has happened in both the legal and medical fields since then. It is also clear that the atmosphere in which the Feversham inquiry was undertaken has now changed and Sir John Peel and his colleagues in contrast to Lord Feversham were under no pressure to recommend that AID be banned. As it turned out Lord Feversham and colleagues recommended that AID should be discouraged but they did not take the further step of recommending that it be declared criminal or prohibited by law.

The wheel has now turned full circle and the basis of Sir John Peel's recommendations is that AID should be allowed and that it should be provided free under the National Health Service. Perhaps this is bowing to the inevitable, for although Lord Feversham was able to say categorically in 1960 that AID was not carried out in National Health hospitals, the same cannot be said today. Seven members of Lord Feversham's committee recommended that there should be no change in the laws of legitimacy to accommodate the birth of a child conceived by artificial insemination thus making the child illegitimate. But now, quite properly, Sir John Peel's panel comes out strongly in favour of changing the laws relating to legitimacy so that such a child would be legitimate. In so doing the panel gives support to the two dissenting members of Lord Feversham's committee, who although not wishing to encourage AID felt that the child should not have to bear the stigma of illegitimacy. But what is the demand for AID? Some 1,400 marriages a year are childless because of the husband's infertility, according to Sir John Peel's panel, but other estimates put this number as high as 4,000 marriages a year. Very few of these couples now have children by AID but as fewer children are now available for adoption, the case for AID becomes stronger. There is also a smaller, but even more necessary, demand for AID in cases where it would be inadvisable for a husband to father a child when for example the husband suffers from a particularly debilitating disease which might be passed on to his offspring.

The state has now been reached where careful consideration must be given to the conditions in which sperm is obtained from donors for insemination. Little attention has been given in the past to test the donor for the presence of genetic or other diseases and personal acquaintance with the donor has been taken as enough evidence of the donor's suitability to donate sperm.

*British Medical Journal Supplement, April 7, 1973.

But with the practice of AID on the increase it must be asked whether this affords enough protection for the mother. It is accepted practice in the United States to pay sperm donors and the practice has recently been reported in Britain. But does the payment of donors throw a new light on the practice of AID? It is well known in the United States that the quality of blood obtained for transfusion depends on whether or not the donor was paid. Could the same happen to the quality of sperm if the practice of AID becomes much more widespread? The practitioners of AID are the first to stress the advantages of the technique over adoption. They point out that in contrast to adoption the mother does carry the child for nine months and a normal mother-foetus relationship develops. But whether AID is provided under the National Health Service or not there is a patent need to clarify the legal situation surrounding children born as a result of artificial insemination by donor. The child so born is illegitimate and the husband who hides the fact by appending his own name as the father in the registry of births is in strict law committing perjury. Surprisingly though it may seem the legal situation of the donor is far from clear—does he have the same responsibility in law as the father of an illegitimate child and also can the child lay claim to the estate of the donor? Whether or not AID is provided under the National Health Service in Britain it must be accepted that the technique is proven and will continue to increase in popularity. But the legal anomalies surrounding AID must be removed as soon as possible.

100 Years Ago

AN Icelandic gentleman sends to the *Scotsman* an account of the eruption of the Skaptar Jokull in Iceland, which took place in January last. On January 9, about three o'clock A.M., there was observed from Reykjavik a great fire in the E.N.E. The fire shot up like lightning, displaying beautiful evolutions in combination with the electricity above. So bright was it, that during the dark morning hours it was thought it must be very close to Reykjavik. But when daylight dawned, and the mountains could be discerned, a thick and heavy column of vapour or steam was observed far in the background, beyond all the mountains, so that it was clear that it was far off, and, according to the direction, it seemed most likely to be in Skaptar Jokull, the west part of Vatna Jokull—the great waste of glaciers in the east and south of the island. Morning and night this grand display was visible during the 9th, 10th, 11th, and 12th, and during the day the column of steam and smoke stood high in the sky. All agreed that the eruption must be in Skaptar Jokull, and from various observations it was concluded that the position of the crater ought to be between 67° 7′ and 67° 18′ deg. north lat., and 30° 45′ and 30° 55′ west long. from the meridian of Copenhagen. In the east, near Berufjord, some shocks were felt, and fire was seen from many farms. Ashes, too, had fallen over the north-east coast so abundantly that pasture fields were covered, and the farmers had to take their sheep into the huts and feed them.

From Nature, **7**, 470, *April 17, 1873*

OLD WORLD

Lord Bessborough Delivers Several Telling Blows

GOVERNMENT research establishments should not normally undertake repayment work for industry, according to the Committee of Enquiry into the Research Associations which reported this week. Lord Bessborough's committee feels that research associations by their long and intimate contact with industry are better equipped to undertake work of industrial importance than most of the government establishments. (*Industrial Research and Development*, Conference of Industrial Research Associations, £3.00.)

But even where the work requires equipment and expertise not found within the appropriate research association so that the only appropriate place to do the research is a government establishment, the committee says that the research association concerned should be brought into the management of this activity. The committee is particularly concerned about the role that the Atomic Energy Research Establishment at Harwell is now playing in undertaking contract research for British industry and it suggests that the establishment should be subjected to greater control.

It is clear that Lord Bessborough and his colleagues would prefer to see Harwell converted into a large research association but they reluctantly admit that such a conversion "would be cumbersome". It would be preferable they say, to break the establishment down into "separate research association-type units". Alternatively the facilities at Harwell could be transferred to existing research associations. But Harwell is not the only government establishment to come under attack, and the management of the ship division at the National Physical Laboratory appears in a far from good light. The British Ship Research Association carries out its ship towing work at the ship tank at the NPL, and, according to the report, "the relatively uncoordinated way" in which NPL conducts its ship tank work makes "BSRA's planning, programming and project control very difficult".

The solution, according to Lord Bessborough is for the management of the ship tank to be transferred from the NPL's hands to BSRA. This, according to the report, would be in "the best national interest", but a merger of BSRA into NPL, which has been suggested in the past, would not be desir-

able. It is argued that as the research association's chief interest is to serve their industry and as the NPL's objectives are to serve "more loosely defined national requirements", marriage of the NPL and BSRA would not be effective. But it is, perhaps, the shipbuilding industry's reported wish not to be buried within a national laboratory that carried most weight with the committee.

The committee comes out in support of the customer-contractor principle but it feels that it is not wise to "carry a general principle to an extreme". Support is also given to the government's decision, made last autumn, to abolish the grant-in-aid system to research associations, although the committee recognises that this will put several research associations under financial pressure. A general grant, according to the report "can insulate the recipient from commercial pressures and lead to a lack of initiative and commercial enterprise." In the same context the committee welcomes the recommendation made by the Select Committee on Science and Technology in their third report last year that contracts between industry and

government research establishments should not be subsidized out of public funds.

The report recognizes that to substitute fees for contract research for the sums presently received as a grant is not going to be satisfactory for the associations and it recommends that the government should continue to contribute monies other than for contract work.

Lord Bessborough also says that if more had been invested in research and development in the "bread and butter" industries rather than in "glamorous high technology", then "perhaps our balance of payments history and recent economic progress might have been considerably improved".

The committee feels, however, that the research association systems is easily justified. In 1970 the research associations spent £17 million supporting industrial technology, which is about 2.5 per cent of the amount spent within private industry on research and development. The government contributes £4 million a year to the research associations, which is 0.7 per cent of its total expenditure on research and development. Neverthe-

EUROPEAN RESEARCH

Advice for the European Commission

THE first meeting of CERD, the European Commission's unofficial advisory body on all matters scientific, went off last week with a lengthy discussion on the committee's objects and a convoluted attempt to define pure and applied research.

The twenty-one man committee, whose membership includes scientists, industrialists and representatives of research councils, all of whom are there in their own right rather than as representatives of their governments, is to advise the commission on all matters relating to research and development that fall within the commission's scope. The committee's opinions will be canvassed before the commission officially formulates its policies, and meetings will take place at least twice a year and more frequently if necessary

Last week's meeting was judged highly successful in Brussels, although differences in approach, ranging from the Rothschild-like theory that research should only tackle specific problems to the more European line that an overall science policy should be created, had to

be ironed out. The meeting ended with each country retiring to decide which areas are in need of research and their proposals will be discussed at the next meeting of the committee. The British members of CERD are Sir Brian Flowers, Chairman of the Science Research Council, Dr John Kendrew, MRC, Cambridge, and Lord Kennet. The committee's chairman, at least until the commission appoints a full-time scientific adviser, is Professor Hendrik Casimir, Director of Philips and the commission's current scientific adviser. Other members of CERD are: Barry, V. C. (Dublin), Bertin, J. (Plaisir, France), Bölkow, L. (Munich). Braans, C. M. (Jutphaas, Holland), Caracciolo di Forino, A. (Rome), Danzin, A. M. (Versailles), De Gennes, P. G. (Orsay, France), Della Porta (Milan), Demeester, M. (Brussels), Janssen, D. (Brussels), van Lieshout, R. (Hague), Lüst, R. (Munich), Metz, P. (Luxembourg), Peccei, A. (Rome), Rasmussen, P. N. (Copenhagen), Weissermel, C. (Frankfurt), Winterfeld, K. E. (Lyngby, Denmark).

less, according to the report, "overall, the money devoted to research associations has produced handsome benefits for industry and the economy".

The organization of food research in Britain also comes in for attack. The committee points out that there is no overall view taken by the government of food research activities and that there are no formal means of communication between the food research associations and government, Agriculture Research Council stations and the universities which are involved in food research. This has led to duplication of effort and overlap of research. The food research associations also complained to Lord Bessborough of a "lack of openness" on the part of government stations. The committee of enquiry suggests that all basic work done on food research at government and other institutions should be fed to the industries through the research associations.

The ARC spends about £18 million a year while the food research associations in 1970–71 spent only £365,000. ARC representatives sit on certain research association bodies but reciprocal arrangements are rare. The report even goes so far as to state that friction exists in some cases between the research associations and other institutes involved in food research. In spite of all these apparent disadvantages the committee reflects that it is the research associations rather than the ARC "which are more directly meeting the needs of the consumer".

EUROPE

Mergers Good and Bad

THE recent decision to merge the two nuclear power consortia in Britain was a move that will not benefit Europe, according to Mr Christopher Layton, lately *chef de cabinet* to Mr Altievo Spinelli, one of the Italian European commissioners, and now Director for Advanced Technology Industries at the EEC commission. Mr Layton was addressing a conference last week at the University of Sussex on cooperation in research and technology in Europe.

It would have been much better, said Mr Layton, if the British consortia had separately merged with other European nuclear power companies. If they had done so the Central Electricity Generating Board would not have been faced with the prospects of buying British or foreign—a choice that is now inevitable. Instead, it could have chosen between the rival claims of two companies each of which would have had a strong British representation.

Mr Layton came out strongly in favour of wholesale mergers of European companies in order that European industries can effectively compete with

companies in the United States and other parts of the world. In particular, Mr Layton thinks that there should be two strong computer companies in Europe. Siemens and Philips will soon bring out a common range of computers but ICL will not join with these companies because it has "a different philosophy". But the EEC would like to see ICL find a partner in Europe, and Mr Layton suggested that Nixdorf, the German company, might be suitable.

But computers and nuclear power are not the only fields where Mr Layton wants a few strong European companies, and he also mentioned the aircraft industry — "we've got Concorde and we cannot go on like that"—telecommunications, railways and the heavy electrical industry. But Mr Layton was not clear whether the EEC policy is to encourage one or more large companies within Europe in any given industry. In some fields it might turn out to be essential to have only one consortium to compete effectively with companies in the United States. It might turn out that this is essential in the computer industry but first Mr Layton would like to see two companies set up.

Euratom came in for some severe criticisms at the conference. First, Mr Layton said that much of Euratom's programme had failed and then Professor Christopher Freeman, of the Science Policy Research Unit at the University of Sussex, said that there was "clear evidence of considerable doubt" with the performance of this organization. Eldo was also criticized by Professor Freeman but he was loud in his praise of CERN. The success of CERN can be directly attributed to the fact that the organization and the users worked closely together. In fact, said Professor Freeman, an analysis of the success and failure of twenty or so European collaborative ventures in research has shown that no project can hope to be successful without it having a well defined objective and without it having a market for its end product.

Professor Freeman spent some time in detailed criticisms of the work of the MIT team on modelling the environment and economic conditions of the world. In spite of the detailed disagreement between him and Professor Dennis Meadows and colleagues, Professor Freeman stressed that mathematical simulation models are useful research tools and that where he diverges from the conclusions of the MIT team is in thinking that such models cannot as yet be used as guides for science policy.

But it was clear from the conference that the strong national feelings within the European Economic Community have not been removed by these countries signing the Treaty of Rome and that a lot more than legal pressure is needed to break down these barriers.

ENVIRONMENT

European Cooperation

CLOSER cooperation on European environment policies and a work list for the Council of Europe emerged from a meeting of 17 West European environment ministers held in Vienna recently. At the end of the meeting at which 23 countries, some of them non-member states of the Council of Europe, discussed ways and means of preserving the natural environment, resolutions were passed calling for a greater exchange of information between member states. "Close cooperation between governments is necessary in relation to national environment policies in Europe, and legislative and administrative actions and controls should be harmonized wherever possible," the ministers said.

The ministers also resolved to avoid duplication of work on the natural environment by examining the studies that are already being run by international organizations.

They also asked the Council of Europe to look into the possibility of drawing up a legal instrument to define the rights of the individual to an improved environment and to define his responsibilities within it.

Three formal resolutions were drawn up dealing with the management of the natural environment, the conservation of flora and fauna and the dissemination of information about the environment. All three involved work for the Council of Europe.

Lists of endangered species will have to be drawn up and the council will undertake specific studies of areas such as the Mediterranean. At the end of the meeting, and under considerable pressure from Mr Geoffrey Rippon, Britain's Secretary of State for the Environment, the ministers agreed to meet in Brussels in 1975 and in Switzerland at a later date to review progress towards a European conservation policy.

Stoned in Brussels

BRITAIN may be in Europe and the European Commission may be furiously "harmonizing" everything in sight, but language remains obstinately unharmonizable. At last week's meeting of CERD (see page 427) one of the German delegates, speaking in his own language, inserted an aside to the effect that "Einstein war ein grosser Forscher" (Einstein was a great research scientist) which the French interpreter stolidly translated as "Une pierre était un grand chercheur". The non-German speaking French delegates looked a trifle blank.

NEW WORLD

United Nations' Science Policy Checked

by our Washington Correspondent

Two years ago, the Economic and Social Council of the United Nations established a high level committee to plan and coordinate UN policies for bringing science and technology to bear on the problems of developing countries. Called the Committee on Science and Technology for Development, it was launched in the hope that it would provide a strong and effective voice in the development of UN science policy. But that hope dimmed a little last month when the committee's first meeting got bogged down in a political dispute, failed to tackle most of the items on its agenda and ended in uproar.

Although the political problems which dominated the committee's first meeting could have been predicted in advance, the fact that they squeezed out discussion of virtually everything else came as a bitter blow to several participants at the meeting. In short, the committee got caught up in the broad debate about financial aid to developing countries and, as one delegate put it last week, it provided a forum for "national posturing".

The essence of the debate was that delegates from the developing countries insisted that the committee should concern itself first with the adoption of a resolution calling for specific funding commitments from the developed nations. Those delegations, led by Brazil and Pakistan, urged the committee to recommend three financial targets to be reached by the end of the decade, namely that the developing nations should spend 1 per cent of their gross national products on science and technology, that the developed nations should spend 0.05 per cent of their gross national products on direct aid for science and technology in the developing nations, and finally, that the developed nations should devote 10 per cent of their national research and development budgets to problems of the developing nations.

The delegations from the developed nations argued, however, that the committee should not concentrate on financial targets, but should be more concerned with specific projects. The discussion of that topic occupied the first two-and-a-half weeks of the three week meeting, and finally it was put to a vote—in itself a highly unusual procedure since agreements at such UN committees are usually reached by consensus. The vote was neatly split with the delegates from developing nations voting for the funding recommendations, the delegates from Western developed nations voting against them and the delegates from the Communist countries abstaining. Since the developing countries had a majority the resolutions were passed.

Why were attitudes so rigid that the debate was allowed to carry on for almost the whole meeting, finally ending in a vote whose outcome could have been predicted on the first day? The answer can only be found in the context of other UN committees and activities, according to several sources concerned with the meeting.

At centre stage is a document called the International Development Strategy for the Second United Nations Development Decade, a blueprint on international aid during the 1970s which was adopted by the UN General Assembly. The strategy provides for review of its provisions every two years, the first of which is now getting under way in earnest. A Special Committee on Review and Report will meet in the summer to consider recommendations on updating the strategy from several other committees, including the Committee on Science and Technology for Development, and it will send its own resolutions on the strategy to the Economic and Social Council. Ultimately, the General Assembly will consider the resolutions.

The Committee on Science and Technology for Development thus represents part of the first stage in updating the strategy, and the delegates were anxious to establish their national postures so that their views would carry to the next committee layer. According to a member of the UN Secretariat concerned with the science committee, the postures will perhaps soften at each stage of the review, and it is thus simply unfortunate that the committee's first meeting should have provided the forum for such a tactical battle. That viewpoint was confirmed by a delegate from a developing country, who preferred not to be named, who said that the insistence on funding commitments "was a necessary exercise in the light of the calendar of meetings".

As for the funding targets themselves, the chief bone of contention was the third provision, that the developed nations should spend 10 per cent of their research and development budgets on problems of the developing nations, drawn up in consultation with those nations. Delgates from the developed countries resisted the proposal for several reasons, only one of which is that for some countries it would represent a significant increase over present spending. Perhaps the chief argument was simply that there are no criteria by which to determine what research is of benefit to developing countries.

Dr Frederick Seitz, President of the Rockefeller University and leader of the US delegation, said last week that the discussion over the third target was really "tilting at windmills". He said that he believes that it would be easy to demonstrate that the United States, the United Kingdom and several other Western countries spend at least 10 per cent of their research and development budgets on problems of benefit to the developing countries, but that little thought has gone into drawing up the relevant criteria. Consequently, the US delegation offered a resolution, which was finally agreed to after revisions, requesting the Secretary-General to convene a group of experts to undertake such a task, and to present its recommendations to the next meeting of the Committee on Science and Technology for Development.

The view of the US delegation, and of most other delegations of the western developed countries, was that in the absence of such criteria it is fruitless drawing up funding recommendations and the committee should concentrate on specific projects. Another member of the US delegation said last week that "if a good project is proposed, money will be found for it".

A member of the British mission to the UN said last week that he was "very disappointed" that little of substance emerged at the meeting, and in particular pointed out that there was no discussion of the future work of the committee, or of its role in relation to other committees of the UN. He added that since the committee got off to such a poor start, many countries may be unwilling to send such top level delegates to future meetings. Dr Seitz was also disappointed at the concentration on funding targets, but said that he was not too surprised at the way things turned out. Nevertheless, "If the next meeting is as fruitless, then I shall be very disappointed", he said.

The delegate from a developing country was more sanguine, however, suggesting that the resolutions on fund-

ing will cause the developed nations to think much more closely about the orientation of their research and development budgets, and will help promote more cooperation between developing and developed countries on science and technology. He added that now the question of funding commitments has been settled, albeit by a vote which did little to change attitudes, the committee can get down to the "more exciting" discussion of projects in its next meeting.

Perhaps the most fitting comment on the meeting was provided not by the delegates, but by the translators. After the meeting had dragged on past the time at which they should have left, the translators walked out, leaving a number of delegates talking in a variety of languages until the chairman finally gavelled the meeting to a close.

HIGHER EDUCATION
Job Prospects Improving

by our Washington Correspondent

THOSE who are about to leave universities in the United States with a first degree will find the job market better this year than at any time in the past four years, according to the latest report from the Carnegie Commission on Higher Education. The commission also believes that job prospects for first degree holders will be fair for the rest of the 1970s and improve in the 1980s. Nevertheless, about a quarter of the new college graduates will find themselves in jobs which have not previously been filled by graduates and of those, about half will have to accept jobs which will not make use of their college education.

The outlook for holders of a PhD is, however, much more grim. The commission reckons, on the basis of a thorough review of masses of statistics, projections and analyses, that the job market for PhDs will perhaps worsen towards the end of the decade and become even tighter in the 1980s. But, while there is likely to be a large surplus in some disciplines, such as the humanities, there may even be a shortage of PhDs in engineering and some of the physical sciences.

The Carnegie Commission's report (*College Graduates and Jobs*, McGraw Hill Book Company, Highstown, New Jersey 08520, $4.50) presents a vigorous rejection of the suggestion that "manpower planning" should be the basis for planning the development of higher education, suggesting that such an approach is not feasible or desirable in a decentralized economy such as that of the United States. In general, the commission argues that the federal government should not respond to the tight job market of the past few years

by shutting off a variety of student support programmes, and that there is no basis for predictions of "gloom and doom". In fact, the report states that although there will be a temporary glut of graduates in some fields, there will be no "major overall crisis—at least for a long time to come".

The report is the latest in a series of reports and analyses put out by the Carnegie Commission and by a variety of other institutions all of which have been concerned at least in part with one overriding concern—a complex web of factors has created the greatest financial crisis that universities in the United States have ever experienced. Most of the reports have ended up by arguing that changes in attitudes are needed by educators, employers and government officials to cope with the financial crisis and, as far as the job market is concerned, the Carnegie Commission is not alone in recommending against restricting entry into the universities because of a perceived lack of job opportunities for graduates.

In short, what has happened in US higher education is that in the late 1950s and early 1960s the universities underwent a massive expansion, force fed by grants from federal and state governments. Between 1950 and 1970, undergraduate enrolments increased from 2.1 million to 6.8 million, while enrolment for graduate courses shot up from 220,000 to 940,000 in the same period. In most fields the demand for both first degree holders and for those with advanced degrees outstripped supply until a general economic recession set in in the late 1960s.

Partly in response to the high unemployment rate among graduates (which, nevertheless, has remained lower than that of non-graduates) many federal programmes in support of higher education, such as the traineeships and fellowships administered by the National Science Foundation, began to dry up in the early 1970s. Consequently, virtually every university in the United States has been caught in a tight financial squeeze and many have had to cut back on enrolments and staff hiring, and even to drop some courses. And the higher education act amendments, passed by Congress last year, have turned out to be less of a saviour for the universities than many had hoped (see *Nature*, **234**, 65, 1971).

What lies in store for those emerging from the universities with newly minted degrees in the next few years? According to the Carnegie Commission, the economic recession is abating and although predictions about the labour market are difficult to make, the United States "appears to be moving towards a favourable employment situation". The report states that the output of college graduates will probably increase

by about 50 per cent on the 1970s compared to the doubling of the 1960s, and the job market should be better than it was between 1968 and 1973, but worse than in the 1960s.

The commission takes note of predictions from the US Bureau of Labor statistics that "a high school education will be sufficient for 8 out of 10 jobs" during the 1970s and points out that in fact one-third of the 18 to 21 age group is in college at any one time. Consequently, the commission reckons that at a very rough guess, between 1 and 1.5 million new graduates will have to take jobs each year for which a college education is not required.

As for the market for PhDs, the slowing down in the growth of undergraduate enrolments and in university expansion in general has already severely cut back on the number of teaching vacancies and other job opportunities in the universities. This trend will continue and will cause severe problems in the PhDs job market in the late 1970s and 1980s, the commission warns.

The report suggests that the universities and state governments should respond to this situation by preventing the spread of PhD courses to institutions that do not now have them and problems in the PhD job market in existing graduate schools should not be started up without good cause.

A task force established by the Department of Health, Education and Welfare, headed by Dr Frank Newman, Director of University Relations at Stanford, also expressed grave concern recently about the recent trends in postgraduate education in the United States, suggesting that the shift in enrolments from institutions of acknowledged excellence to new institutions has given rise to a "threat to the overall quality of graduate training of scholarly research". The Newman task force also suggested that federal cutbacks in training grants and fellowships are hitting hardest in the high quality institutions, thereby tending to reduce overall quality of postgraduate education. The task force's chief recommendation was that postgraduate students rather than universities should be supported by direct, portable grants which they would be free to take to the institution and course of their choice.

As for scientists and engineers, the Carnegie Commission's report suggests that there is a strong possibility that shortages will again develop soon for engineers and graduates in some of the physical sciences. This is partly a consequence of the fact that enrolments have dropped off recently partly in response to the highly publicized unemployment of engineers in industries particularly affected by the economic recession.

NEWS AND VIEWS

More Questions than Answers at East Rudolf

RESULTS of field work in the East Rudolf area of Kenya continue to expand knowledge of the evolutionary development of man, but as Richard Leakey has pointed out in a recent issue of *Nature* (**242**, 170 ; 1973), more questions are now arising than are finding answers.

Because of Leakey's insistence on the representation of a wide variety of geological, palaeontological and anatomical specialities East Rudolf continues to be one of the best known early man locales. Even the continuing difficulty in obtaining further reliable radiometric dates has not been a severe handicap because other methods of dating the sites are now available. Maglio's attempt (*Nature*, **239**, 379 ; 1972) to correlate the East Rudolf fauna with that from other radiometrically-dated sites in East Africa seems a particularly good application of a dating method which, in other circumstances, has been justly criticized.

Leakey's report in this issue (see page 447) brings abundant affirmation of the lower Pleistocene (if not Pliocene) existence of the genus *Homo*. The large, and now reasonably complete calvarium, KNM-ER 1470, re-iterates what more fragmentary and less dramatic material from the East Rudolf area has been suggesting for some time. The postcranial material, including two nearly complete femora, also re-emphasizes and clarifies the early hominid dichotomy. The comparatively large size of this skull, the lack of strongly developed or continuous brow ridges, the vertical parietals and other morphological features of the cranium quite clearly place the specimen outside the australopithecine grade of evolutionary development. In view of other evidence from past seasons, especially the KNM-ER 730 and 820 jaws and the KNM-ER 737 femur, the early existence of *Homo* at East Rudolf is no surprise. Although no dental measurements accompany this preliminary report it is interesting that the recently discovered "*Pithecanthropus* VIII" skull in Java shows apparently similar mesiodistal compression of the cheek teeth and a short, broad palate as are seen in the new Rudolf skull. The zygomatic process of the maxilla also appears to show a similar conformation in the two specimens.

One of the big bonuses of the East Rudolf material is the collection of associated material—associated in the sense of two or more bones having come from a single individual. Although definitely associated cranial and postcranial material has not yet been discovered at any lower Pleistocene hominid site, several related limb bones are now known from the Rudolf area. The body of evidence now available indicates that australopithecine locomotion, although clearly bipedal, did not necessarily conform to a hypothetical transitional model between apes and man. It now seems possible that the locomotive behaviour of these early hominids may have been different from any known pattern. The suggestion that the forelimb may have been long in relation to the hindlimb is interesting and may stimulate work which will eventually clarify one of the most elusive aspects of studies of early man.

The question which the new material really poses is what should now be done, in a taxonomic sense, with the gracile australopithecine and "*Homo habilis*". "*H. habilis*" has been suggested as a direct ancestor of modern man, yet, more than a million years later than KNM-ER 1470, the habilines from Bed I at Olduvai Gorge have a smaller endocranial capacity and a cranial morphology perhaps more primitive in some respects than the Rudolf skull. Although it is dangerous to put too much emphasis on brain size alone (living *H. sapiens* has a range of more than 1,000 cm²) the quite advanced morphological pattern of the new skull clearly suggests that it is not australopithecine.

It may well be, as Leakey has suggested elsewhere, that the East African material presently suggested to be from gracile australopithecines should be re-allocated. The very wide diversity found in this group would mean that some specimens would be placed with the robust australopithecines and some specimens would be placed with *Homo*. This would clarify and simplify the situation seemingly revealed by the postcranial bones. In the lower limb there is clear evidence of two types of erect and efficient bipedality. But if two types of australopithecines are recognized in East Africa then the mounting evidence of contemporary *Homo* could demand three types of lower limb morphology; this is not indicated in the East Rudolf material.

There is a further and perhaps sometimes overlooked implication of the East Rudolf material. It can no longer be doubted that two types of hominids co-existed in East Africa; if the Chesowanja skull (Carney *et al.*, *Nature*, **230**, 509 ; 1971) is accepted as the latest (and last) evidence of that co-existence then the period of sympatry was at least 2 million years. This firmly and unequivocally indicates that the australopithecines were not incompletely evolved or inefficiently adapted hominids, as some workers have suggested; it is indicative of a very high level of adaptation and development that two closely related hominids were able to co-exist successfully for such a period.

From our Palaeoanthropology Correspondent

"Gating Currents" in Axons

IT is generally accepted that the action potential of nerve cells and muscle fibres arises from a transient increase in the ionic permeability of the surface membrane which in turn leads to a transient inward movement of positive ions. Since the pioneer work of Hodgkin and Huxley (1952) the ionic currents have been measured in a variety of experimental conditions ; ionic permeabilities and their dependence on voltage and time have been extensively studied. The ultimate aim has been to obtain information

about the events which, on a molecular level, cause the transient increase in membrane permeability. Considerable efforts, both experimental and theoretical, have been made to elucidate the molecular events (see the review by Keynes, *Nature*, **239**, 29 ; 1972) ; in spite of these efforts, however, the molecular basis of the permeability changes has essentially remained a mystery.

The characteristic property of an (electrically) excitable membrane is the marked dependence of its ionic permeability upon voltage. The simplest explanation would be that charged particles (for example, the flexible polar ends of certain phospholipid molecules) alter their position in the membrane according to the electrical potential across the membrane, thereby opening or closing pathways ("gates") for ions such as Na⁺ or K⁺. This hypothesis has an important consequence: the opening of the ionic "gates" should itself produce a small membrane current which precedes or parallels the sodium or potassium current and is caused by the displacement of the charged particles inside the membrane. This "gating current" should be proportional to the number of "gates" and the amount of charge transferred at each one. Because of its small size it should be seen best in the absence of the normal ionic currents.

The search for the hypothetical "gating current" became an exciting task for axon physiologists. As the years passed by, the hunt grew more and more intense ; new methods such as signal averaging and intracellular perfusion of giant axons improved the chances for solving the problem. Chandler and Meves (*J. Physiol.*, **180**, 788 ; 1965) found no evidence for a "gating current" within the limits of their instrumental sensitivity, whereas unpublished experiments by H. M. Fishman (see footnote in Jain *et al.*, *Proc. US Nat. Acad. Sci.*, **67**, 799 ; 1970) seemed to indicate a positive result. On page 459 of this issue of *Nature*, Armstrong and Bezanilla describe "currents related to movement of the gating particles of the sodium channels".

Armstrong and Bezanilla used the voltage clamp technique to carry out their experiments on intracellularly perfused squid giant axons. The ionic currents were reduced to a minimum by using a sodium-free external and a potassium-free internal solution. The capacitative and the leakage current were eliminated by algebraically summing the currents from equal pulses of opposite sign. This was done by a signal averager which averaged the currents from several thousand pulses of each polarity. The current remaining after this procedure was a transient outward current at the beginning of the clamp pulses and a transient inward current at the end of the pulses. The current transients (which have a superficial similarity to recently published records from the frog muscle, see Schneider and Chandler, *Nature*, **242**, 244 ; 1973) are interpreted as "gating currents". This interpretation is supported by measurements of the area under the current transients which, for strong pulses, corresponds to 300 electronic charges per μm² of membrane ; assuming six charges per gate one arrives at 50 gates per μm², in reasonable agreement with estimates derived from studies of tetrodotoxin binding to other axonal membranes. A great deal more work is, however, required until one can be sure that the current transients described by Armstrong and Bezanilla have something to do with the opening and closing of the "sodium gates".

The experiments of Armstrong and Bezanilla justify

the hope that the problem of the excitable membrane may eventually be solved along the lines that have been indicated. Another report about new experiments on squid axons (see Landowne, on page 457 of this issue of *Nature*) seems more difficult to reconcile with present ideas about the function of the nerve membrane. The voltage clamp studies of Hodgkin and Huxley (1952) showed that low temperature prolongs the duration of the permeability changes without appreciably interfering with the magnitude of the permeability increases ; therefore a large increase in the net ionic movement during activity was predicted for low temperatures. The expected increase in potassium loss at low temperatures was subsequently found (Shanes, *Amer. J. Physiol.*, **177**, 377 ; 1954), but the effect of low temperature on sodium entry was never investigated. The experiments by Landowne are concerned with this question. The results are, however, quite unexpected: they show a clear decrease (rather than the predicted increase) of sodium entry during activity at low temperatures.

There are probably several ways to explain the apparent paradox. Landowne chooses the most radical interpretation by saying that his data "seem to rule out any model of the nerve membrane which accounts for the current by a simple change in permeability". He develops an alternative model based on the assumption that the amount of sodium which enters the fibre during the nerve impulse is limited to the amount of sodium stored inside the surface membrane before the impulse ; the amount of stored sodium is assumed to decrease with decreasing temperature (see also Hoyt and Strieb, *Biophys. J.*, **11**, 868 ; 1971). It is interesting to note that this model does not seem to require the existence of "ionic gates" and "gating currents". The full justification for the far reaching theoretical conclusions is difficult to judge ; it seems, however, certain that "Landowne's paradox" will stimulate further experimental work.   H. M.

Neuronal Plasticity

ONE of the most interesting and poorly understood phenomena in neurobiology concerns the nature of neuronal plasticity and of the trophic influences exerted by neurones on innervated structures. Recent studies have revealed that selective changes occur in the synthesis of well-defined macromolecules in adrenergic cells in response to changes in neuronal activity, suggesting that such cells may provide a valuable model for biochemical studies of these processes. It has been found that the activity of cholinergic nerves supplying adrenergic neurones in sympathetic ganglia or adrenal chromaffin cells partially controls the synthesis of the key biosynthetic enzymes tyrosine hydroxylase and dopamine-β-hydroxylase in these adrenergic cells (for review see Molinoff and Axelrod, *Ann. Rev. Biochem.*, **40**, 465 ; 1971 ; Thoenen, *Biochem. Soc. Symp.*, No. 36, 3 ; 1972).

Neuroblastoma cells, derived from a mouse tumour of adrenergic origin, have been widely used as an *in vitro* model system for studying the factors which control neuronal development and differentiation. Such cells, unlike normal neurones, grow and divide rapidly in tissue culture, although their genetic heterogeneity leads to considerable morphological and biochemical variations among

individual cells. This latter problem has to some extent been overcome by the systematic isolation and analysis of a variety of neuroblastoma of clonal origin (Amano, Richelson and Nirenberg, *Proc. US Nat. Acad. Sci.*, **69**, 258 ; 1972). Some clones give rise to cells containing extremely high activities of the enzyme tyrosine hydroxylase, and one of these "adrenergic clones" has been used by Richelson (*Nature New Biology*, **242**, 175 ; 1973) to examine the control of the synthesis of the enzyme tyrosine hydroxylase.

Richelson confirms the previous finding (in a similar but less active neuroblastoma preparation) of Waymire, Weiner and Prasad (*Proc. US Nat. Acad. Sci.*, **69**, 2241 ; 1972) that the addition of dibutyryl cyclic AMP causes approximately a doubling in the activity of tyrosine hydroxylase. The new study shows, furthermore, that this change in enzymatic activity represents both an increase in the specific activity of the enzyme (per milligram protein) and an increase in the total amount of enzymatic activity per cell. This is an important point, because Richelson also confirms (as reported by Waymire *et al.*, 1972) that sodium butyrate — a possible metabolic product from dibutyryl cyclic AMP — causes an increase in the amount of tyrosine hydroxylase per cell, but not in its specific activity.

Sodium butyrate seems to inhibit cell division. In the normal growth of neuroblastoma cells in tissue culture, formation of the enzyme occurs largely after the log phase of growth is completed ; by arresting cell division butyrate seems merely to accelerate the normal processes of biochemical differentiation occurring in the cultured cells. When cells were cultured with reduced amounts of foetal calf serum, so that cell division was not encouraged, butyrate no longer had any effects, although dibutyryl cyclic AMP was still effective. The actions of dibutyryl cyclic AMP were enhanced by the phosphodiesterase inhibitor theophylline. Prostaglandin E_1, however, which has been reported to increase the concentration of cyclic AMP in neuroblastoma cells, did not cause any marked increase in tyrosine hydroxylase activity. The results, nevertheless, strongly suggest that cyclic AMP may play a part in the biochemical differentiation of neuroblastoma cells, and, by inference, of adrenergic neurones. Addition of dibutyryl

cyclic AMP has also been shown to influence other aspects of the morphological and biochemical specialization of neuroblastoma cells (Prasad and Hsie, *Nature New Biology*, **233**, 141 ; 1971 ; Furmanski, Silverman and Lubin, *Nature*, **233**, 413 ; 1971).

The implications of Richelson's findings in neuroblastoma cultures have been supported by recent results obtained with normal adrenergic cells. Addition of dibutyryl cyclic AMP to organ-cultured mouse and rat sympathetic ganglia leads to increased synthesis of the enzymes tyrosine hydroxylase and dopamine-β-hydroxylase in the adrenergic neurones of these ganglia (Mackay and Iversen, *Brain Res.*, **48**, 424 ; 1972 ; Keen and McClean, *Arch. Pharmacol.*, NS, **275**, 465 ; 1972). In such isolated ganglia, the stimulation of tyrosine hydroxylase activity by nerve activity *in vivo* can be simulated by the addition of substances such as potassium chloride that cause a depolarization of the adrenergic neurones. These effects are enhanced by theophylline, suggesting again an involvement of the cyclic AMP system in mediating the control of enzyme synthesis by depolarizing stimuli. Such an involvement is also supported by the finding (Guidotti and Costa, *Science*, **179**, 902 ; 1973) that conditions leading to increased tyrosine hydroxylase activity in rat adrenal medullary chromaffin cells *in vivo* are

associated with an increase in the concentration of cyclic AMP in such cells. The phosphodiesterase inhibitor aminophylline also promotes an increase in the cyclic AMP content and in tyrosine hydroxylase activity in these cells.

The biological ramifications of the adenylate cyclase-cyclic AMP control system know no bounds. A role in controlling neuronal plasticity, however, is at least a relatively novel regulatory function for this ubiquitous messenger substance.

From our Neuropharmacology
Correspondent

GROOMING MOVEMENTS
Endogenous Control

from our Animal Behaviour Correspondent

DURING the past ten years, considerable interest has centred on the effects that various sorts of feedback from an animal's own movements or sounds have on the subsequent development of complex species-specific patterns of behaviour. White-crowned sparrows, for example, need to hear the sound of their own voices if they are to develop the proper song characteristic of their species. When white-crowned fledglings, which have been exposed to their species song, are deafened before they themselves have started singing, they subsequently produce highly abnormal songs (Konishi, *Z. Tierpsychol.*, **22**, 770; 1965). They thus seem to need to hear

Reverse Transcriptase of Chick Cells

IN *Nature New Biology* next Wednesday (April 18) Kang and Temin report new data which add support to their claim to have detected in chick embryo cells an RNA-dependent DNA polymerase ; in other words a reverse transcriptase, which is biochemically and serologically distinct from the reverse transcriptase present in avian RNA tumour viruses. Last year Kang and Temin reported (*Proc. US Nat. Acad. Sci.*, **69**, 1550 ; 1972) that chick cells contain an endogenous reverse transcriptase associated with an endogenous RNA template. They showed that this activity is sensitive to RNase, resistant to DNase, partially resistant to actinomycin D and makes a DNA complementary to the associated RNA. They failed, however, in their initial attempts to isolate a RNA/DNA hybrid intermediate made by this chick endogenous reverse transcriptase.

By varying slightly the method of isolating this endogenous reverse tran-

scriptase activity, Kang and Temin have now succeeded in obtaining preparations which *in vitro* synthesize DNA and give rise to an RNA/DNA hybrid, the RNA moiety of which is sensitive to RNase and alkali and can be heat denatured. Furthermore, they obtained evidence which suggests that the DNA chain of the hybrid may be covalently linked to an RNA primer molecule. These properties of the RNA/DNA hybrid molecules made by this activity are reminiscent of the RNA/DNA hybrids made at early times by reverse transcriptase of tumour viruses, but the endogenous enzyme of chick cells and the enzyme in avian RNA tumour virus particles are different molecules. As Kang and Temin say, these data "suggest that endogenous RNA-directed DNA polymerase activity is not unique to viruses, and virus-infected or tumour cells". What role the endogenous reverse transcriptase of chick cells plays remains a fascinating question.

themselves practising. There are other cases, however, where no such feedback is apparently necessary: chickens deafened soon after hatching give all the normal species calls (Konishi, *Z. Tierpsychol.*, **20**, 349; 1963).

Fentress has now given a particularly clear demonstration of a complicated sequence of movements developing in the absence of obvious feedback (*Science*, **179**, 704; 1973). The grooming movements of mice are characteristic of the strain to which the mouse belongs and have several definable components which follow each other with a fair degree of regularity. The forepaws sweep over the snout and various parts of the face and contact the tongue in a complex pattern. Mice which have had one or both forepaws amputated at birth so that they have only stumps also "groom": they sit in the hunched posture characteristic of a normal grooming mouse; their tongues, shoulders and stumps move just as if they had functional paws. They show the same increase in amount of grooming that normal mice do during their third week after birth, and the normal coupling between shoulders and tongue movements occurs even though the tongue has no paws to lick. Most striking of all, the shoulder traces out large amplitude sweeps over the eye and the eye closes at just the right time even though there is no paw there to touch it. The sequence of movements is also similar. Normal mice go from licking to single rapid strokes along the snout and the mice with amputated paws also show this transition.

Although there may, of course, be subtle as yet undetected differences between normal and pawless mice, it is clear that what might be thought an essential stimulus, namely, the touch of the paws on the face, is not necessary either for the development or for the execution of a complex series of movements involving several parts of the body.

TISSUE CULTURE

Fun with Cytochalasin B

from our Cell Biology Correspondent

ADDING a dash of cytochalasin B to cultures of mammalian cells and watching what happens seems to have become a diverting pastime for many cell biologists, and there is no denying that this interesting drug causes cultivated cells to undergo remarkable changes. Perhaps the most dramatic and ultimately useful property of cytochalasin B is that it can, when used in appropriate conditions, cause the enucleation of most cells in a population. Goldman, Pollack and Hopkins (*Proc. US Nat. Acad. Sci.*, **70**, 750 ; 1973), for example, by ingeniously

harnessing centrifugal force with cytochalasin B, have obtained populations of enucleated BSC-1 cells and BHK-21 cells attached to coverslips and their data clearly indicate that these enucleate cells are viable. They can, for instance, be removed by exposure to trypsin solutions from the coverslips and then replated whereupon they resume the typical morphology of cultivated fibroblasts (BHK-21 enucleates) or epithelial cells (BSC-1 enucleates).

Obviously the enucleates must contain whatever information, in other words, molecules are necessary for attachment, spreading and form. The enucleates are also capable of pinocytosis and locomotion ; they are susceptible to contact inhibition of locomotion, and Pollack and Goldman have apparently shown that they support virus replication. Presumably, therefore, there is in the cytoplasm of these cells sufficient amounts of the macromolecules involved in these various processes to allow them to continue for several hours after the loss of the nucleus. And one does not need much imagination to devise interesting experiments that exploit that fact. What, for example, happens when enucleate cells are infected with transforming viruses or fuse enucleate cells of one sort or another to nucleated cells using inactivated Sendai virus to mediate fusion? Such experiments should be fun to do and the results may even be rewarding.

Defendi and Stoker (*Nature New Biology*, **242**, 24 ; 1973) have recently drawn attention to another useful property of cytochalasin B, namely its ability to induce general polyploidy in populations of BHK-21 cells and presumably cells of other lines. Regardless of whether or not the target of the drug is a cells microfilament system, and that is a vexed question, in appropriate conditions it causes the nuclei of BHK-21 cells to divide but prevents cytokinesis, the division of the cytoplasm. As a result binucleates accumulate and when the drug is removed many of these binucleates undergo a further round of DNA replication before mitotis and cytokinesis so that many cells emerge tetraploid. As Defendi and Stoker point out, although many drugs induce polyploidy by interfering with the mitotic spindle cytochalasin B induces polyploidy without drastically reducing viability. It ought, therefore, to be possible to use the drug to induce polyploidy in experiments designed to test how the chromosomal constitution of a cell affects the expression of phenotypic characters. In particular it should be possible to exploit cytochalasin B to test the idea, championed by groups led by Harris, by Pollack and by Sachs, that a cell's chromosome balance regulates its tumorigenicity.

In short cell biologists now have at

hand a drug that can be used to yield viable enucleates or viable polyploids. The bags from such a happy hunting ground should be considerable.

BACTERIA

Colicide

from our Molecular Biology Correspondent

THE colicins are proteins, secreted by strains of *Escherichia coli,* which have the property of rapidly and specifically killing various related bacteria. This phenomenon has been examined at a number of structural and biochemical levels: in the best documented case, that of colicin E3, the site and nature of the lethal act have now been established, and a certain amount is known about how the intruder insinuates itself into the cell. The target of colicin E3 is the 16S RNA of the smaller ribosomal subunit, which it severs near the 3' end, with consequent annihilation of biosynthetic function. There are some odd aspects of this reaction, in particular that the colicin will not attack isolated RNA, or even the lone 30S subunit. This can in principle be explained in terms of ribosomal conformation, which, as a variety of independent lines of evidence suggest, undergoes some sizable change when the subunits dissociate ; it has also been suggested, however, that the colicin is not in itself a nuclease, but rather a regulator of a dormant nuclease already present on the ribosome. Some evidence in favour of the first explanation now comes from Dahlberg *et al.* (*Biochemistry,* **12**, 948 ; 1973).

They find that the cleavage of the 16S RNA by the colicin is subject to inhibition by some antibiotics which are known to operate directly on the ribosome. Thus streptomycin, which binds to the ribosome, deranges the assembly of the polypeptide chain, with apparently an accompanying structural disturbance, will prevent cleavage of the RNA by the colicin in streptomycin-sensitive, but not in resistant cells. Two other antibiotics, which are not thought to have the same ribosomal binding site as streptomycin, function similarly, both *in vivo* and *in vitro*. This argues strongly in favour of stringent conformational requirements that specify the circumstances in which the colicin E3 will interact with the 30S subunit. Dahlberg *et al.* report that the selfsame scission of the 16S RNA occurs also when *Bacillus stearothermophilus* ribosomes are exposed to colicin E3, although the sequence at the 3' end is quite different from that in *E. coli*. This too then apparently reflects a structure-dependent specificity. Two antibiotics, erythromycin and also kasugamycin, which is known to interact with the 16S RNA at the 3' end, that is to say, in the very

region attacked by colicin E3, do not interfere with colicin inactivation.

Confirmation that the attack on the 16S RNA is indeed the lethal event, rather than any action in the membrane, for example, that might precede it, comes from Samson, Senior and Holland (*J. Supramol Struct.*, **1**, 135 ; 1972), who find that protein synthesis is arrested some five minutes after the addition of colicin E3 to the culture, and that the cleavage of the RNA, as followed by gel electrophoresis, occurs over about the same period. There is in fact some indication that protein synthesis continues for a few minutes after cleavage, perhaps until completion of the polypeptide chain. A curious observation is that a small amount of the 3' terminal fragment, or at least something indistinguishable from it electrophoretically, appears to be present even in cells that have not been exposed to the colicin.

The other colicins, E1, E2 and K, which are also proteins of about 60,000 molecular weight, do not evidently attack the ribosomes, and may act instead on the membrane. Like E3, they must have the ability to enter the cell, in spite of their large size. Direct observation of some form of mayhem by colicin E1 in the *E. coli* membrane is described by Phillips and Cramer (*Biochemistry*, **12**, 1170 ; 1973). The fluorescence of the lipid-soluble molecule, anilinonaphthalene-sulphonic acid (ANS) in the *E. coli* membrane is slightly shifted and considerably enhanced on addition of colicin E3, and the same is true of the less polar, and presumably even more lipophilic species N-phenylnaphthylamine (NPN). The cells can be rescued from the effect of colicins by addition of trypsin within a short period after exposure to the colicin, which is presumably destroyed on the surface before its ingress into the cell. Phillips and Cramer find that the fluorescence enhancement lags behind the absorption of the colicin measured in this way. The colicin E1 induces leakage of potassium and a drop in intercellular ATP concentration. This, however, is not the cause of the fluorescence change, for the perturbation is not affected by prior exposure to a reagent that causes the ATP level to be sustained. The simplest interpretation of these events is that the colicin brings about a cataclysmic change in the membrane when it enters, which affects permeability to potassium ions or ATPase activity.

In an accompanying article, Cramer, Phillips and Keenan (*ibid.*, 1177) adduce more evidence that the fluorescent enhancement of the NPN is a structural effect, for the Arrhenius plot for the kinetics of the increase show a break that corresponds to the temperature of the membrane phase transition to a more fluid state, this depending on the temperature of cell growth, which in turn

governs the phospholipid composition of the membrane. There seems also to be a small change in fluorescence polarization, and hence mobility of the fluorescent marker. The passage of the colicin into the membrane thus seemingly depends on the nature of the bilayer.

The colicins have specific membrane receptors, which evidently participate in their passage through the bilayer, and Sabet and Schnaitman (*J. Biol. Chem.*, **248**, 1797 ; 1973) have now achieved substantial purification of such a protein. The colicin E3 binding activity passes into a detergent-soluble fraction on disruption of the membranes, and can be further purified by ion-exchange chromatography. Not only does it bind the colicin, but the complex is precipitated by a colicin-directed antiserum. Moreover, the protein is missing in colicin E3-resistant cells. Sabet and Schnaitman estimate that there are some 220 molecules of the receptor per cell. The similarity between the colicins is strikingly underlined by the observation that the colicin E2 binds to the same receptor. Colicins E1 and K, however, do not bind. The receptor activity for these species is also solubilized by the

detergent, but does not remain with the E3 and E2-binding activity after fractionation. There are reasons for postulating that E1-receptor activity might involve the same protein (or actually glycoprotein, for carbohydrate residues are implicated) in combination with some other component.

PLANT GEOGRAPHY

Success and Fall

from our Plant Ecology Correspondent

MUCH effort has been expended on tracing the geographical origins of domesticated plants and animals. Many species have been transported far from the places in which they evolved and their responses to climatic factors have been greatly modified by selective breeding. This makes it difficult to determine their origins from their physiological attributes. Weed species have certain features in common with crop plants; they too have been carried far from their points of origin. often to regions of differing climates. Weeds, however, have not been subjected by man to such rigorous selective pressures

Where the Rhodopsin is Not

A RECENT article by Dratz *et al.* (*Nature New Biology*, **237**, 99 ; 1972), purporting to show that rhodopsin is completely buried within the rod outer segment membrane has drawn criticisms from Vanderkooi, and a rejoinder from Dratz and Schwartz. In the original article the inaccessibility of the rhodopsin at the aqueous interface of the membrane was inferred by the failure of reactive side chains to react with a covalent labelling compound incapable of penetrating into the bilayer. By contrast, rhodopsin liberated by disruption of the membrane reacted copiously. Vanderkooi points out, in next Wednesday's *Nature New Biology* (April 18), that there could be other reasons for low reactivity than physical occlusion. He notes that other workers have found reagents capable of reacting with rhodopsin side chains in the membrane, supposedly without entering the bilayer. He also draws attention to a large body of X-ray diffraction evidence which is united in the one respect that the rhodopsin is only partly immersed in the membrane, and projects out of it into the aqueous medium.

In an accompanying communication, Dratz and Schwartz reject Vanderkooi's arguments, but not apparently his conclusion that their inferences were wrong. They suggest that published results on specific labelling referred to by Vanderkooi are also ambiguous, because some reagents can · penetrate the bilayer and others have a geometry that may

enable the reactive group to project into the bilayer and there react. They then refer to work of their own, and others, given at a recent meeting of the Biophysical Society, which indicates that part of the rhodopsin is in fact available to reagents in the aqueous medium. They have also calculated electron density profiles across the membrane for various dispositions of the rhodopsin, and do not seem to find good agreement with experiment for any of the models, including that for totally buried protein: here the shape is right (which it usually is), but the quantitative fit is poor.

The dispute may help to clarify the limitations in the use of labelling reagent for membrane proteins. includes an implicit admission of error in the earlier work, but makes no impression on the problem of rod outer segment membrane structure.

An article by Phillips and Morrison in the same issue of *Nature New Biology* emphasizes the complexity of reactivity of membrane components. Iodination of red cell membranes under the action of lactoperoxidase leads to labelling of only two proteins, which are therefore accessible at the surface. The new results show that after mild treatment with trypsin, which releases surface glycopeptides, the same two proteins take up much more label. This is interpreted in terms of a protective carbohydrate barrier on the outer membrane surface.

and their physiological requirements can occasionally offer a clue to the climatic conditions and hence the geographical situation of their origins.

Thompson (*Ann. Bot.*, **37**, 133; 1973) has examined the germination characteristics of the weed *Agrostemma githago*, the corn cockle, with the intention of tracing its origin. Thompson has already established that the temperature requirements of seeds for germination vary according to the climatic conditions under which the species evolved (*Ann. Bot.*, **34**, 427; 1970). A surprising outcome of this earlier work was that species of Mediterranean origin germinate at lower temperatures than those from northern Europe, a feature of selective value in a situation where the most unfavourable period for establishment and growth is during the dry, hot summer. Germination in the winter allows establishment to occur well before the physiological stress of summer.

Thompson has found that *Agrostemma* has the germination characteristics of a Mediterranean species; even at 0° C there is moderate germination. Its distribution in Europe is now widespread as a result of dissemination with cereal seed, which it closely resembles in size. Probably its association with cereal cultivation is as old as agriculture itself. Its success as a weed can be associated in part with the germination characteristics which *Agrostemma* had evolved in response to its native Mediterranean climate. It can germinate very early in the spring and soon after ripening. These features, in addition to its very high viability, have made the species a successful opportunist.

In spite of many adaptive features the success of *Agrostemma* as a weed species has declined markedly during the past hundred years. In the nineteenth century the plant was an abundant weed in cornfields in Britain, but by the early part of this century it had become far scarcer. This decline coincides with the introduction of more rigorous screening of cereal grain, which has reduced the likelihood of re-introduction of *Agrostemma* with each year's sowing. This cannot fully account, however, for the virtual elimination of the species. One must also explain its failure to maintain a viable population derived from earlier introductions. Here the Mediterranean adaptations which Thompson describes may once again provide the answer. Germination at low temperature in autumn in British conditions can result in the exposure of seedlings to the severity of winter, which a Mediterranean species is not adequately fitted to withstand. It is ironic that the very characteristics which led to the success of *Agrostemma* may now have contributed to its downfall.

MARS

Polar Wandering?

from our Geomagnetism Correspondent

THE possibility of terrestrial polar wandering (as opposed to continental drift) has been under discussion for many years now, although a firm conclusion one way or the other has yet to be reached. In the meantime, however, Murray and Malin (*Science*, **179**, 997; 1973) are already speculating on the possibility of polar wandering on Mars, on the basis of Martian features revealed by Mariner 9.

What Murray and Malin consider to be the most "suggestive" evidence comes from the quasi-circular topographic features observed in the polar regions of Mars. These features were recently described by Murray *et al.* (*Icarus*, **17**, 328; 1972) as near-circular plates with outward sloping edges and comprising thin (20–80 m) lamellae of light and dark material. Because they form generally concentric patterns and occur only in polar regions, it is tempting to relate their origin and subsequent history to the position of the Martian spin axis, the assumption being that they formed symmetrically about the rotational pole. But what makes them particularly interesting from the point of view of polar wandering is that they seem to form a series of offsets. Thus if the polar origin assumption is valid, the implication is that the poles have also undergone displacement.

The association of the topographic features and their laminated terrain with the poles also implies an association

with the polar carbon dioxide "frost" which appears and disappears on an annual cycle. This, in turn, implies a genetic relationship with volatiles and thus leads to a natural explanation for the polar symmetry. The idea here is that the volatiles may collect atmospheric dust before being lost by sublimation. The symmetry of the topographic features about the spin axis may therefore represent the annual stability boundaries of the volatile carbon dioxide. In other words, the behaviour of the polar-related carbon dioxide appears to leave a visible trace which may be used to determine any polar motion. On this basis, the plates clearly visible indicate a polar motion of about 15°.

A second line of argument is based on the strong evidence for extensive volcanic and tectonic activity on the surface of Mars—in particular, the discovery by Mariner 9 of large constructional volcanic features with a general morphology similar to that of terrestrial shield volcanoes and located near the equator in the longitude range 90°–150° W. The largest of these features corresponds to the previously-known albedo feature Nix Olympica, although three others, about 400–550 km in diameter and about 10 km high, were recognized for the first time from the Mariner 9 photographs. There is also evidence of many smaller volcanic features scattered over the surface of Mars.

The presence of volcanic activity on Mars does not in itself imply polar wandering but, as Murray and Malin point out, it is instructive to determine whether or not the extrusion of such a large mass of material could have pro-

Frameshift Suppressor Transfer RNA

FRAMESHIFT mutations arise from the insertion or deletion of a nucleotide, or any number of nucleotides other than three or multiples of three, into a gene with the result that the reading frame of all triplet codons distal to the mutation is changed. Such mutations can be internally suppressed if a compensatory mutation occurs in the same gene. For example, a frameshift mutation resulting from the insertion of a base is suppressed by the deletion of a neighbouring subsequent base. Frameshift mutations can also, however, be suppressed if a transfer RNA molecule is mutated so that it can read non-triplet codons in which case suppression is said to be external. Several external suppressor mutations of frameshift mutations of the histidine operon of *Salmonella typhimurium* have been isolated and one of these external suppressor mutations, the *sufD* mutation, has now been characterized by Riddle and Carbon.

In *Nature New Biology* next Wednes-

day (April 18) they describe an elegant set of experiments which establish that the *sufD* mutation is located in a structural gene for a species of glycine tRNA which reads the codon GGG. Their experiments also prove that the tRNA molecules specified by *sufD* mutants have an anticodon sequence CCCC instead of the anticodon sequence CCC present in the wild type tRNA. This tRNA might therefore translate frameshift mutations which involve the change of a GGG codon to a GGGG quadruplet or the additional base in the tRNA anticodon may "simply serve as a spacer, so that the tRNA occupies an unusually large space over the message and so suppresses +1 frameshifts". But whatever the mechanism, the striking fact Riddle and Carbon have found is that certain frameshift mutations resulting from the addition of a single base are suppressed by a species of tRNA carrying an additional base in its anticodon.

duced a rigid body nutation. In fact, calculations show that the Nix Olympica mass, for example, is likely to give a rigid body nutation of only 0.04°. Thus even the effect of the four largest shield areas will be at least two orders of magnitude smaller than the polar wandering implied by the quasi-circular polar features. But is Mars a totally rigid planet? The fact that the observed value of the primary coefficient of the low order harmonics of the Martian gravity field is close to that expected from a rotating planet in hydrostatic equilibrium suggests that, although Mars has a rigid surface, its interior may be hot enough to support viscous motion. In this case, the nutation could be much higher than that predicted on the basis of a rigid body. Moreover, the presence of viscous motion itself implies mass movements much greater than those represented solely by the exposed shields. The existence of what amounts to mantle convection would be consistent with polar wandering but, as in the case of the Earth, would not be sufficient to prove it.

A third feature of Mars relevant to the polar wandering argument is that the low degree spherical harmonic coefficients (non-hydrostatic) of the gravity field are relatively larger than those of the Earth. On Mars they also correlate significantly with surface topography and geology, whereas they do not do so on Earth. Thus, for example, the apex of the equatorial bulge for both the gravity field and the planetary surface correlate well with the location of the four large shield volcanoes. This phenomenon could be taken to support the connexion between large-scale volcanism and deep-seated density differences which would be expected at the start of large-scale mantle convection, although, perhaps unfortunately, an interpretation could also be made in terms of a totally rigid Mars. To this extent, the gravity data are equivocal.

Nevertheless, at least three different aspects of Mars are at least consistent with polar wandering. But if polar wandering has taken place, or is taking place, what is its rate? The equatorial shield areas contain few impact craters, and so they are probably no older than a few hundred million years. This gives a rough idea of the time scale involved. The polar features may, however, give a more accurate result. Assuming, as Leighton and Murray (*Science*, **153**, 136 ; 1966) did, that each lamella of the laminated terrain represents a 50,000-year climatic period, the clearly distinguishable polar plates may represent about 5×10^7 yr, and the more eroded plates offset from the present axis by up to 20° may represent about 10^8 yr. On this basis, the polar wandering rate would be about 5×10^{-9} rad yr^{-1} or about 20 arc min per million years.

NUCLEAR STRUCTURE

Testing New Models

from a Correspondent

THE study of nuclear physics has long since fissioned into nuclear structure and high energy physics, a division which is formally recognized in conferences such as that held in Liverpool from March 28 to 30 under the auspices of the Institute of Physics. (In turn there has appeared to be subdivision within nuclear structure physics too, but the boundaries seem less clear.)

At the Liverpool conference Dr R. Chapman (University of Manchester) surveyed the evidence for a dramatic departure from the rotational model sequence of energy levels which occurs at high angular momentum in heavy nuclei. This phenomenon is now ascribed to a phase change in the nucleon motion from that of a superfluid to that of a near rigid rotor. Thus from failures of simple models much is learnt about the physics of the nucleus. The same general point was mentioned by Dr R. R. Whitehead (University of Glasgow) in the very different context of large-basis shell model calculations for light nuclei. By ingenious computational techniques and the use of large

computers it is now possible to make traditional shell model calculations for nuclei in the 2s-1d shell without resorting to the usual pruning of smaller wavefunction components. Dr Whitehead argued that whereas it was possible to contrive agreement between model and experiment by using effective nuclear forces to cover up for a truncated calculation, a better idea of the real nuclear forces would be learnt from the success or failure of the fuller calculations.

Although recognizing the importance of these mammoth calculations, many physicists—and especially experimenters — feel the need for a complementary simple model whereby they may grasp some meaning from the various data over a range of nuclei. Dr P. W. M. Glaudemans (University of Utrecht) described such a model for s–d shell nuclei using the so-called surface–delta interaction. Although this schematic model is nominally of the shell model type, the effective interaction used enables it to reproduce some of the observed strong electromagnetic transition strengths which betray the presence of collective nuclear motion.

The experimental evidence for such collective motion in s–d shell nuclei has grown rapidly in the past few years.

Explaining Electric Detonation of Explosives

ALTHOUGH it is well known that solid explosives can be detonated by electric fields and electric discharges, it is not clear just what mechanisms are at play in the process. Some have suggested that, in the case of azides like $Cu(N_3)_2$, the explosion can be traced back to a breakdown of electrical resistance caused by the injection of holes from the anode or of electrons from the cathode. Another question that arises is whether mechanical shock or thermal shock arising from the electrical breakdown is responsible for the triggering of the explosion.

In next Monday's *Nature Physical Science* (April 16) Chaudhri describes a study by means of high speed photography of the early stages of this kind of detonation. The figure shows a sequence of photographs taken at a rate of 5 million frames a second of the stages in the decomposition of a single crystal of silver azide (AgN_3). A negative pulse of amplitude 10 kV and rise time about 0.5 μs was applied between frames 2 and 3, and it reached a maximum between frames 4 and 6. Two dark expanding regions S and S_1 are in evidence in frame 6, and, significantly, they are well away from the electrodes. The later frames suggest that the dark regions arose from shock waves. Chaudhri says, however, that it is not clear whether the shock waves he observed are the

result of electrical breakdown or the initiation of fast decomposition at these points.
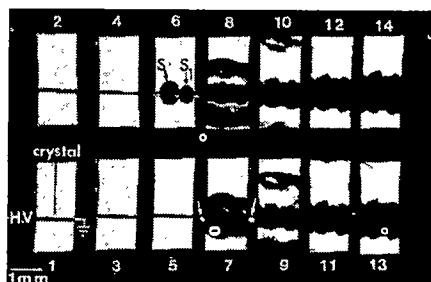
The electrical initiation of a reaction in a crystal of AgN_3. The electrodes are steel plates. The single crystal is $\sim$ 100 μm in diameter, and the whole arrangement is situated in a container filled with oil.

Another sequence of photographs, this time taken at a rate of 10 million frames a second, reveals an initial dark spot in the crystal near, but not at, the anode. It would seem that the propagation speed of the reaction was some 1,750 m s^{-1}, about 70 per cent greater than the normal propagation speed. Chaudhri concludes that the reaction does not start because of impact ionization and decomposition by electrons injected from the cathode, but he says that more work will have to be done to pin the mechanism down.

Some pattern is emerging from the welter of data obtained, chiefly as a result of improved detection, electronics and on-line computing facilities. Dr P. J. Twin (University of Liverpool) showed examples of the combined power of the measurement of lifetimes, X-ray angular distributions and polarizations in elucidating the level schemes of these nuclei. The broad overview is that the nuclei around Mg are deformed and prolate with a change to oblate shape at around ^{28}Si. So the systematics here reveal shape transition, a phenomenon which has motivated much work previously on heavy nuclei.

Dr P. G. Hansen (University of Aarhus and CERN) described some sophisticated experiments at CERN on nuclei well off the stability line. For example the isotope effect has been measured for several neutron-deficient mercury isotopes. This seems to follow the simple dependence on neutron number of a straightforward volume effect down to ^{185}Hg where there is a distinct break. A sudden onset of nuclear deformation might explain this but it has not been confirmed by independent evidence. The Scandinavian workers have been speculating on the existence of the bubble nucleus. This would be spherical but would have a small hollow centre and it would favour high angular momentum states.

Professor J. de Boer (University of Munich) gave a handyman's guide to the principal features and parameters of heavy ion Coulomb excitation. This process affords direct measurement of nuclear electric multipole matrix elements. Current interest is in the measurement of static quadrupole and transition hexadecapole moments which are tell-tale signs of the nuclear charge distribution.

By virtue of parallel sessions it was possible for anybody to contribute. There was also time to hear Professor H. Frohlich (University of Liverpool) and Dr N. MacDonald (Glasgow) elevating biology by bringing to that field—with humour and effect—some methods of theoretical physics.

NMR

^{13}C and Avenaciolide

from our Chemical Physics Correspondent

FOR many years isotopic labelling with radioactive ^{14}C has been widely used in biosynthetic studies and it is not immediately obvious why anybody should prefer to use the stable isotope ^{13}C. Yet this is precisely what Tanabe, Hamasaki, Suzuki and Johnson (J. Chem. Soc. Chem. Commun., 212; 1973) have now done in their study of avenaciolide (see diagram). In its biosynthesis by the metabolite

Aspergillus avenaceus they have used in the feedstock ^{13}CH$_3$COONa and, separately, CH$_3$^{13}COONa, and have confirmed that the C$_8$ side chain and principal skeleton have the expected alternating origin for the carbon atoms; 1,3,5,7,9, and 13 are derived from the CH$_3$ groups and 2,4,6,8,10, and 14 from the $-$COO$^-$ groups. They have also confirmed that the adjacent atoms 11 and 15 may both come from the CH$_3$ sites as would be expected if they were derived from the central atoms of a succinic acid intermediate.
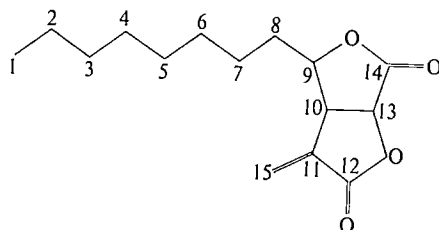
Structure of avenaciolide.

The ^{13}C atoms in the product are, nowadays, readily detected with a Fourier transform NMR spectrometer with proton decoupling facilities. This technique greatly improves the signal-to-noise ratio of the record, first because signals are detected from all the ^{13}C nuclei throughout the measuring time instead of the resonances being recorded separately one after the other; the information is then unscrambled and presented in regular spectral form by a computer. Second, the improvement arises from the

collapse of a multiplicity of peaks into a single line of the same total strength, which occurs because all the influence of the carbon–proton spin-spin coupling is removed from the spectrum. Although the sensitivity is even then poorer than that of radioactive tracer work with ^{14}C, it is quite sufficient provided that the biosynthetic growth process does not involve appreciable dilution of the feed material.

When the ^{13}C technique is applicable it has several established or potential advantages. First, all labelled positions can be identified from the chemical shifts without the need for any chemical operations comparable to the selective degradations required to establish the site of ^{14}C. Second, in principle the enrichment of each site can be determined from the signal strength. Third, the technique is non-destructive and so the product is available for further use. Fourth, for substitution at adjacent sites the carbon–carbon spin-spin coupling can be used to identify such double labelling. In other words, the technique can distinguish a mixture of the type ^{12}C$_a$$-^{12}C_b$ and ^{13}C$_a$$-^{13}C_b$ from a mixture of the types ^{13}C$_a$$-^{12}C_b$ and ^{12}C$_a$$-^{13}C_b$ and indeed could detect and quantify a mixture of the last three species. Fifth, in multiple labelling experiments it could distinguish ^{13}C–D from ^{13}C–H and also ^{13}C$-$^{15}N from ^{13}C$-$^{14}N groupings. With these attractive features it will be surprising if ^{13}C labelling is not exploited to a great extent in future biosynthetic experiments.

Stellar Nucleosynthesis and the s-Process

THE importance of the short-lived s-process chronometer ^{205}Pb, its relation to the mechanism of s-process nucleosynthesis and its implications for cosmochronology are discussed by Blake, Lee and Schramm in next Monday's Nature Physical Science (April 16). So far, the only reliable indicators of nucleosynthesis timescales are for the r-process, which proceeds rapidly by neutron capture and yields, ultimately, very heavy elements such as ^{235}U and ^{238}U. The s-process, of course, also proceeds by neutron capture, but slowly by comparison with the associated β-decay process, chiefly involving light elements initially and building up to, for example, Sr, Zr and Pb.

The importance of finding an s-process "chronometer" lies in the estimate it would provide of the time between the solidification of Solar System material and the end of the sequence of events which produced the element abundances observed in the Solar System.

One of the important links in the chain of element building occurs in the lead-thallium region (see diagram).

Here, there is a possible branching of the s-process at ^{204}Tl; this is shown by dashed lines in the figure, where r denotes r-process, s denotes s-process, and c indicates cosmogenic origin.
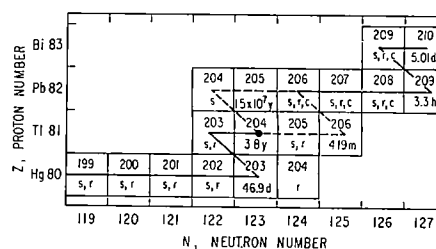
The most probable s-process site is in the interior of red giants. According to Blake et al., the time scale for the s-process is comparable with that derived from the r-process, so that all Solar System material from all nucleosynthetic sources separated over the same time, between 0.7 and 1.1×10^8 yr according to present estimates. With better measurements, this should provide an insight into the processes involved in the formation of the Solar System.

Uncertainties in Energy Policy

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This article describes the factors that affect the way in which Britain's fuel needs are met.

Two sets of problems are posed by the present energy situation. The first is concerned with the supply fuels of all kinds available to meet British requirements and their relative cost. The second group relates the British situation to conditions in the European Community, the United States and the world generally. Any discussion of any energy policy for Britain must take place within the perspective of the world situation both as regards price elasticities in particular markets, and more broadly in relation to global resources and their pattern and rate of use. As Britain begins to familiarize itself with the implications of the new political imperatives of Community policy harmonization and coordination, the questions to be answered in formulating a British energy policy inevitably involve external factors and their impact on national policy making.

Policy Ingredients

The ingredients of a British energy policy are a mixture of indigenous and imported fossil fuels together with a relatively small quantity of nuclear energy, the balance of payments cost of the former and the opportunity costs of the latter. The proportions in which they are put together, the methods by which they are produced, and the degree of choice open to the consumer, have varied according to political and economic pressures over the years. The common factor has been the continuing tendency for the demand for electricity to double every ten or eleven years, and that for petroleum for motor transport to rise by 5 per cent a year. If this rate of increase is extrapolated transport will have moved up to take 30 per cent of total energy in the year 2000, compared with 15 per cent today. Up to now the market has been left to vary the proportion of the increasing total needed to be met by coal or oil, with nuclear energy in a long-stop position turning out some 9 per cent of the total electricity generated.

On the supply side the dominant factor has been the relative cost of coal and oil, with coal losing out to the readily available supplies of cheap oil which appeared on the market as a result of the discovery and development of new reserves in the Middle East and Africa from the middle 1950s onwards. One result of making cheapness one of the chief policy priorities has been increased dependence on imported fuel. In 1955 imports accounted for only 14 per cent of British energy consumption, by 1970 the figure was 45 per cent. In the EEC during the same period the proportion of imports rose from 20 per cent to 63 per cent. Figures of this kind must of course be related to use. The rise in the number of motor vehicles on British roads accounted for a considerable part of the increase. At the same time it would have been less than sagacious to burden industry with high fuel costs by too stringent limitations on the use of oil. A rationalization of the coal industries of Britain and the Six was an essential stage in their post-war economic development. The way in which it was carried out, however, ignored the special problems of the fuel industries. Decisions to switch over from

coal to oil-burning power stations have to be related to the availability and price of fuel over the lifetime of the equipment. This is likely to be of the order of 25 to 30 yr for coal or oil burning plants and 25 yr for a nuclear plant. An appreciable increase in the price of fuel during this period can only be adjusted to at a considerable capital cost. The four-fuel policy (coal, oil, natural gas and nuclear energy) introduced in the White Paper[1] of 1967 has since been overtaken by the discovery of North Sea oil, the advance in the price of imported oil as a result of the activities of the Organization of Petroleum Exporting Countries (OPEC), and the dramatic changes in the international energy situation which have led to an increasing dependence on imported fuel in the United States. British membership of the European Community has introduced a further set of uncertainties into the situation.

The Rome Treaty did not bind the Six to the introduction of a common energy policy, and responsibility for energy matters was divided between the EEC (oil), the European Coal and Steel Community (coal), and Euratom (nuclear energy). Various initiatives, notably those of 1964 and 1968, have been taken by the Commission towards the formulation of a common energy policy, none of which have gone beyond an appreciation of the situation, and the circulation of information and statistics. The emergence of a situation in which the enlarged Community is dependent for 60 per cent of its energy requirements on imported oil has concentrated attention on the need for a common energy policy which would ensure a better utilization of the indigenous fuels of the Community and a more rapid development of nuclear energy supplies. Another aspect of the situation is the demand that the nine should negotiate as one with OPEC and other sup-
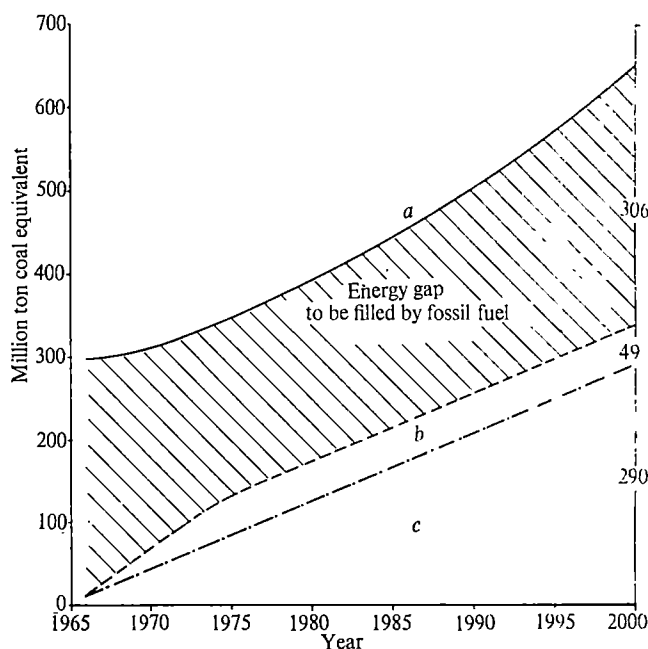
Fig. 1 Projections showing the total fossil fuel energy gap up to the year 2000 for Britain. For 1966 the energy requirement was 297.7 million ton coal equivalent (coal, 174.7; oil, 111.7; nuclear, 10.2; natural gas, 1.1). *a*, Total energy; *b*, natural gas; *c*, nuclear energy. From OECD energy statistics.

pliers of imported fuel. For Britain a Community energy policy poses a number of questions. On the credit side, Community membership opens up the possibility of increased British exports of coal to the rest of the Community. Coal production in the Nine totals some 300 million ton, about a quarter of Community energy requirements. Britain, with an output of some 140 million ton in a normal year, will be able to export increased tonnages to the Continent working up to an estimated 10 million ton.

The prospect of increased sales to other parts of the Community could improve the financial position of the National Coal Board (NCB) by spreading costs over a larger tonnage, and would also reduce its dependence on its principal customer, the electricity supply industry. At the same time the coal industry must now put its research and development programmes into top gear. In the long years during which it began to look as though the only good coal mine was a closed one, there was little incentive to press forward with research into methods of increasing the calorific efficiency of coal.

Today the NCB is able to turn its attention to research and development in both the coal winning and coal utilization fields. The rediscovery of the importance of coal has brought changes in the orientation of this activity. Increasingly research and development programmes in coal are being linked up with those of upstream and downstream interests. This means that machinery manufacturers and users, transport agencies and environmentalists are all interested in new ways of producing and using coal. What is lacking at present is a steady input of information on research and development on other fuels. When this happens and attention is being given to energy resources rather than to individual fuels there will be some hope of securing a coherent energy policy. So far no minister has been in a position to introduce a common research and development policy for energy as a whole, not only in Britain but on a Community-wide basis. Perhaps the increasing urgency of the situation will bring home the fact that competition does not increase the total quantity of finite resources but only their availability.

Each of the fuel industries, meanwhile, is pressing forward with its own research and development programmes. The NCB, for example, has many long and short-term projects designed to fit a situation which calls for increased efficiency in use coupled with reduced pollution. The sort of things that are under investigation are ways and means of increasing the power and reliability of coal-cutting machinery and the introduction of machinery for the automatic sensing of coal seams, able to distinguish between rock and coal. Other areas being studied are the development of smokeless fuel, smoke-eater appliances, and the utilization of colliery shale for structural and other purposes.

The change in the world energy situation which makes urgent policy decisions necessary is the extraordinary growth in demand for energy of all kinds in the past two decades. World energy consumption trebled between 1900 and 1950, a period which took in two world wars, the development of the aircraft industry, and the proliferation of motor transport. Since 1950 world energy consumption has trebled again and the situation now is that world requirements are growing at the rate of 300 million ton of coal equivalent every year. If this rate of increase continues, let alone increases, the possibilities of meeting requirements from fossil fuels are, to say the least, problematical. Gloomy prophesies of coming shortages can be borne with fortitude when it can be assumed that their chief impact will be on other people. The distinctive feature of the present energy situation is that it is making itself felt already in the United States, the world's greatest consumer of energy, where aircraft have been reported to be having difficulty in refuelling at Kennedy Airport.

The causes of the United States crisis are already well known[2]. The significant fact is that the United States will from now on be increasingly dependent on imported energy

and has indeed removed import restrictions on imported oil. In 1970 imports supplied 12% of the energy requirements of the United States, by 1984 they will have increased to at least 30% on present trends. In any discussion of this kind it is all too easy to fly away on a science fiction broomstick and forget that energy demand has to be considered in terms of prices as well as predictions of quantities. Higher prices for Middle East oil not only encourage exploration and development in other areas, but give a new urgency to research into new forms of energy. On the political front the need to bring undeveloped resources into use results in unexpected policy realignments of which the most dramatic so far is the United States/Soviet Union trade agreement of October 18, 1972, which provides among other things for cooperation in exploiting the natural gas resources of Siberia for the benefit of the American fuel economy.

In terms of world energy production oil now supplies nearly half the total (3,050 million ton c.e.) followed by coal (2,500 million ton c.e.) and natural gas (1,300 million ton c.e.). Nuclear energy in 1970, the year to which the above figures refer, provided only 200 million ton c.e. The industrialized countries with the United States at their head, who are responsible for this increase, have only been able to maintain consumption by greatly increasing their imports over a relatively short period. Japan whose energy requirements have risen from 50 million ton c.e. in 1950 to 410 million ton c.e. in 1970, with the expectation that this will double by 1980, has now reached a point where 90 per cent of its fuel requirements are imported.

This upsurge of fuel imports into the industrialized countries has been made up almost entirely of oil from the Middle East and Africa. As far as can be gauged from statements about proved oil reserves this situation, in which one group of countries produce more and more oil to meet ever increasing demand from a totally different group, seems likely to continue. In market terms the members of OPEC are in a position where their long-term interests will be best served by higher revenue per barrel rather than by an increased volume of sales. Libya and Kuwait have already moved in this direction and it seems likely that Saudi Arabia and Iran may decide to conserve supplies also. The host governments' "take" rose by about 50% a barrel as a result of the agreements negotiated with OPEC in 1970 and 1971. It remains to be seen whether these will provide a basis of price stability or whether further substantial increases lie just ahead. A further aspect of the oil supply position is the high cost of production elsewhere in such relatively difficult areas as the North Sea and Alaska. The importance of the North Sea discoveries should not be underestimated, but with production of about 4 million barrels a day in the 1980s it will only be providing about a sixth of the estimated requirements of the Community at that time.

Natural gas provides about a quarter of the energy needs of the industrialized countries. Here again the position is aggravated by shortages in the United States, where reserves are now way below their 1964 level. The importation of liquefied natural gas, particularly into the eastern states will become increasingly necessary. World reserves of natural gas are significantly less than those of oil, and shipments of liquefied gas are only economically feasible at high prices. Release from the world energy dilemma will not come from natural gas, but the geographical distribution of reserves gives an advantage to Britain and other Community countries for the next decade, provided it is not used for purposes for which it is not basically suitable.

After its decline during the cheap energy decade coal is now recognized as having an essential part to play in making up total energy requirements. As one of the world's most plentiful natural resources it could continue to meet its present consumption levels for an estimated 2,000 yr +. Even with consumption increasing at 2% a year reserves would last for 200 yr. There is therefore a secure place for coal in

the energy budgets of the industrialized countries. In Britain this need has been given *de facto* recognition by the government's decision to make grants up to £720 million to the industry over the next five years, and to cancel some £475 million of the NCB's debts. The important feature of this package is not its size but the fact that it acknowledges that market forces by themselves will not produce the required fuel supplies in the right amounts. The grants for particular regions, which amount to £210 million, are not a welfare gesture to keep unprofitable pits going in villages dependent on them for a livelihood, but a means of ensuring that their production will still be available in two or three years on the assumption that oil prices will go on rising.

From what has been said of the fossil fuels it is clear that although a world fuel crisis is likely it is not inevitable. The era of cheap energy in apparently inexhaustible quantities is over. During the 1970s we shall be moving towards a new situation with higher fuel prices acting to keep up the level of supplies, and with increased research activity bringing improvements in the utilization of existing fuels and the discovery of new energy sources. At the same time constraints will be introduced from other motives, for example the opposition by the environmentalists to strip mining at one end of the scale and to the proliferation of nuclear plants at the other. The changing pattern of activity within the energy industries will no doubt produce supplies sufficient to meet the demands of the industrialized countries, at a price. The question is what this price will be not simply in money terms but in social and environmental terms. While the fossil fuels, the world's capital, are being run down, efforts to realize new energy forms, notably solar energy and nuclear fusion, will continue.

As far as Britain is concerned the fact that there is no Community energy policy is an advantage. Britain, with the largest coal production and the as yet unquantified re-

sources of gas and oil in the North Sea, should have a considerable say in future policy initiatives. But this will not be without its problems. One of these is the question of price standardization, which in the case of gas gives a price 30% lower in Lille than at Dusseldorf for gas from Groningen. A related problem is that of the taxation of fuel which varies according to national priorities from one Community country to another. Leaving aside these problems of commercial and fiscal harmonization certain principles for a Community energy policy emerge. The first is that a high priority should be given to security of supplies which means ensuring the maximum use of indigenous fuels. This raises the question of what priority to give to North Sea oil and gas compared with coal and imported oil. The common sense answer would seem to be to use North Sea oil primarily to replace imported oil rather than substituting it for coal in power stations. North Sea gas should not be used extravagantly but conserved by concentrating on premium uses. Nuclear power should be regarded as the long-term takeover fuel and every effort should be made to reduce the capital cost of nuclear power stations and their running costs in order to enhance the competitive position of nuclear electricity. The policy of supporting coal which has been introduced by the British government should continue. In the background but with increasing importance to the solution of the energy problem is the question of research and development. This will clearly have to move on to a Community from a national basis. More importantly it should be concerned with energy requirements as a whole, not with individual fuels. The opening of energy research stations in the Community would be a welcome indication that the scale and significance of the energy problem had at last been recognized.

[1] Cmnd 3438 (HMSO, 1977).
[2] *Nature*, **240**, 249 (1972).

Can Design be Taught?

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Dr Evans examines to what extent "design technology" is a meaningful concept.

I SHALL start by postulating a relationship, namely that design is determined by function and technology. That is, it is determined by what the "machine" has to do and how good a machine can be made in the present state of technology. I use "machine" in its widest sense so that it includes teacups, shovels, baths, computers, kitchens, motor cars, hospitals, houses, roads, cities, and so on. A limitation is set by the materials used to make the machine because the properties of the materials will not only place bounds on the final use to which the machine can be put (for example the temperature it can be used at, or whether it is waterproof or resists corrosion) but will also determine how they can be manipulated in the course of making the machine; they will therefore limit the possible forms the machine can take. The major limitation, however, is

more likely to arise because of an inadequate understanding or definition of the function of the machine or because the user has not decided (where he is free to do so) on the relative importance of the many functions, or has simply not recognized the relative importance of the many functions.

Design is determined by function and technology. So we can make glass houses. But it has to be remembered that people throw stones and, however much the glass is improved, people are not, on that account, going to stop throwing stones. In other words the human element must be taken into account when interpreting the function of the machine, that is, simple mechanistic terms are inadequate.

It is important to maintain a fresh approach here, in particular over the concept of function. Thus the prime function of a machine can be defined, and then any subsidiary functions and the order of precedence of the many-functioned machine. Having done this, one can go on to formulate means of fulfilling this function (but see later) and, inevitably, arrive at a compromise solution. After doing one's own thinking on the problem one can at this stage, but not before, examine any previous solutions that exist and decide how well they fulfil the principal and subsidiary functions of the machine. Any advances in techno-

logy since the realization of these earlier designs (that is, solutions) can then be considered and a more efficient and/or elegant solution produced. I stress the importance of doing one's own thinking when first confronted with a problem (the analysis of function, in the example quoted above) for, if one starts by examining other solutions, one's thinking is inevitably affected by the approach used in the earlier work. It is only by doing one's initial thinking *in vacuo,* as it were, that one can hope to produce new concepts. (There is sound support for this viewpoint from that prolific inventor Sir Henry Bessemer.)

How then can "design" be defined? In general terms I would use "design" as the opposite of "chance" (it has some connotation of imposing order and therefore, in statistical thermodynamic terms, a low entropy state). In the more specific terms of the present context I would define design as the solution to the problem of how to fulfil a recognized function within the limits of our technology. This presupposes, of course, that the elemental function or functions of the proposed machine have been recognized. The ways of doing this will vary somewhat from an individual's solitary "communing with nature on the mountain" to a "brain storming" session by a team.

In recognizing the function or functions of the machine, one enters the realm of analysis. When one comes to formulate a solution one must invoke synthesis. Analysis is essentially a resolving, into component parts of a problem, an idea, or a thing. Synthesis is a "making a whole out of parts". There is, when the two concepts, analysis and synthesis, are set side by side in this fashion a great difference. It is well known, in a general way, that creating is more difficult than destroying, putting together more difficult than taking apart, but I want to propose a semi-quantitative assessment that has not, I think, been suggested before. It is simply this: suppose one can analyse something into six components parts—we have started with an entity, a given thing, and produced six parts. But suppose one starts with six parts, then in general they can be put together in different ways and if the order in which they are assembled is significant then in the limit there are 6! (=720) ways of putting these six parts together. If only one sequence is significant then the chances of hitting on it are smaller than the chances of discerning six parts in a given whole—there is, in fact, a gulf between analysis and synthesis. Whereas analysis has been taught for years under the guise of "the scientific method", the question here is can synthesis be taught? As we must relate our activity to people (it becomes meaningless if we do not) we might start by taking some feasible pattern of life as a base line on which to build, but this is a stifling approach: one must not seek to impose a pattern on humanity. The infinite variety that makes up human activity is to be accepted with gratitude and if people cannot be taught how to design beauty into their machines, as there is no agreement about what constitutes beauty, then they can be taught to design efficiency, comfort (or ease of operation), and safety into the machine. One might hope to add a sense of variety as opposed to undiluted functionalism.

In what ways might one go about this, what are some of the disciplines to be drawn on, and in what new directions should one be looking? The field of ergonomics should be culled (but beware the jargon that sometimes creeps in). The applied psychologists should be consulted and asked to say what they mean in plain English and more experiments should be carried out in this field. A great deal of attention should be paid to spatial relationships, in particular the void must be regarded both as a divisor or separator between solid masses and as a "negative solid". We should consider motif, repetition, pattern, growth and form and the mechanics of growth and form, for example, shells, the different shapes of fish, the thickening of tree branches where they join the main trunk where the bending moment

has its greatest value, and so on.

Virtually all machines (paper weights and door stops possibly excepted, although even they have to be moved into place at least once) have a dynamic aspect and the study of this would be of great importance. It should not be confined to the relative movement of man and machine or fluid and machine, but the flow of people themselves (for example at railway stations, in offices, along paths between campus buildings) or the flow of traffic at different places and at different times and the people/traffic interaction. One should recognize and measure both instantaneous flow patterns and the changing flow pattern over a period (some concepts from solid state physics may be useful here). One must study (or enlarge the studies of) what might be called "proximity effects", that is, how close people can stand other people with whom they only relate in an "average" way (this could be considered an extension of what used to be called by the sociologists "small group dynamics"). One can envisage circumstances where the presence of other people would be reassuring and improve the performance of a task, and circumstances where other people were so close as to irritate and hinder performance. Such studies would have particular relevance in determining the size and layout of buildings in relation to their function.

From here I shall consider size in general. As much of design is by its very nature concerned with the future, attempts must be made to forecast future trends in diverse fields such as population growth, the siting of industry and of new towns, and to identify desirable and likely developments in technology. Here we must not fall into the trap of making an extrapolation (be it linear or exponential) from recent trends. It is indeed essential to reconsider some of the *idèes reçues* on such things as optimum size, and it is to be hoped that the notion that bigger does not necessarily mean better will gain more acceptance. In terms of population growth there is a factor that has been overlooked, but which is very relevant in the present context. To explain it I shall borrow a concept from nuclear physics. This is the concept of "cross-section". Roughly stated, this says that if a particle is moving it takes up more room than if it stays still, that is, it has a larger "cross-section". Now the same can be said of people. A million people in the mid-twentieth century effectively take up more room (and use more natural resources, produce more waste, and so on) than when people were less mobile. Also, continuing to borrow from nuclear physics, the probability of collision increases with increasing cross-section, that is, in terms of people the probability, not so much of physical collision, but of tension and a sense of physical oppression increases with increased cross-section as this adds to the sense of crowding for a given population. Thus, while increased mobility brings greater "freedom" in one sense, it also brings more interaction, thus reducing freedom.

Finally, I shall mention some other areas of interest (the list is by no means exhaustive): the concept of fashion in the use of materials and the "hangover factor", whereby features arising simply from the nature of one material are deliberately copied when a different material is used, for example wood-grained 'Formica' (this can become a legitimate element of pattern or texture) ; the problem of defining scales for design assessment—is this meaningful? ; lessons to be learned by examining national solutions to design, that is, are there any other influences at work besides different life styles, climates, and local materials? ; properties of materials dictate manufacturing techniques and limit design (but "art triumphs over its medium") ; the use of film in teaching (anything), how effective is it? ; form and function, fitness for function, "fun" and function, that is, the inclusion of the apparently irrelevant which has a great effect on the real as opposed to apparent efficiency of the man/machine system—a big potential field for research, and a suitable note on which to end this summary.

Seismic Travel Time Evidence for Lateral Inhomogeneity in the Deep Mantle

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We present evidence from seismic travel time data of lateral variations in the properties of the lower mantle. The size of some anomalies is about 1,000 km.

EVIDENCE from seismic body wave and surface wave data has long indicated that the Earth's upper mantle (depth < 700 km) is strongly laterally heterogeneous. Lateral variations of the compressional wave velocity as large as 10% have been reported for the upper 200 km, and the shear velocity probably varies even more. For depths greater than 700 km, however, the existence of lateral variations has been more difficult to establish, although such variations have been invoked by various workers[1,2] to explain the scatter of some seismological data. Greenfield and Sheppard[3], in a study of $dT/d\Delta$ measurements made at the Large Aperture Seismic Array in Montana, found a pronounced difference between data from events to the northwest and the southeast for epicentral distances greater than 60°, which could not be attributed to the structure beneath the array, and seems explicable only in terms of heterogeneities in the lower mantle. Davies and Sheppard[4] have presented a more extensive collection of data of this type in the form of an "array diagram", on which $dT/d\Delta$ and azimuth anomalies are represented as vectors in slowness space. Many anomalies are found which are too large to be effects of upper mantle heterogeneities in the source regions; on the other hand, the anomalies often vary rapidly with the direction of approach of the waves, implying that structure directly beneath the array is not responsible. Further evidence has come from a study of the diffraction of compressional waves by the Earth's core, in which Alexander and Phinney[5] found that the region of the core–mantle boundary beneath the Pacific Basin is distinctly different from the region beneath the North Atlantic and Africa.

Travel Time Anomalies

We have found evidence that significant lateral variations occur in the lowest few hundred km of the mantle, this region being much more heterogeneous than that which lies above it. The methods of this travel time study are described in detail elsewhere[6].

We restricted the study to data from deep focus earthquakes in an attempt to avoid systematic errors caused by near source velocity variations in the upper mantle, which are particularly severe in seismically active regions. About 3,300 arrival time data from 47 earthquakes with depths between 450 and 650 km were used, all events being located in the deepest parts of their respective seismic zones. For most of the 18 seismic regions involved, two or more events were available, and for each station a consistency check was made to eliminate data contaminated by gross errors. An iterative procedure, similar to the one described by Herrin et al.[7], was then used to determine the earthquake locations, the travel time curve for a 550 km focal depth, and a set of "station corrections" (each represented by a constant) to account for the effect of lateral variations in the upper mantle beneath the stations.
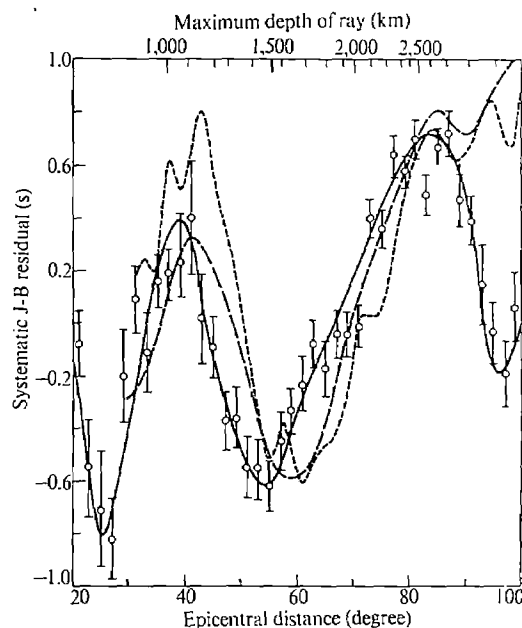
Fig. 1 P wave travel time curve (focal depth 550 km) determined in this study (———), expressed in terms of deviations from the Jeffreys–Bullen values. Data means and their standard errors are indicated for 2° distance intervals. Surface focus curves of Herrin et al.[7] (— —) and Lilwal and Douglas[8] (- - -) have been displaced vertically for ease of comparison.

The travel time curve thus determined is shown in Fig. 1 (in terms of deviation from the standard Jeffreys–Bullen tables), together with the data means and their standard errors for 2° distance intervals. This curve is similar in shape to those found in other recent studies[7,8] except beyond 85°, where most other curves remain approximately parallel to the Jeffreys–Bullen curve, but ours becomes progressively earlier by about 0.9 s. Fig. 2 shows some of the data which have contributed to the determination of the travel time curve; the observed times show a striking dependence upon the location of the earth-

Fig. 2 Travel time data (with station corrections applied) for earthquakes in (*a*) the Sea of Okhotsk and (*b*) Argentina. The solid line is the curve derived from all data.

variations near the focus are further ruled out because early arrivals beyond 85° are not restricted to observations of deep earthquakes; they also occur, for example, in data from nuclear explosions in the Marshall Islands[9].

Deep Mantle Structure

It seems, then, that lateral variations of compressional velocity in the middle or lower mantle are required to explain the travel time anomalies. But because of the uneven distribution of seismological observatories and deep earthquakes, the sampling of the mantle provided by available data is uneven, and it is impossible to determine uniquely the complete three dimensional velocity structure of the mantle. What can be determined is the average travel time residual for each of a number of "bundles" of rays following nearly identical paths from a seismic region to a group of stations, and from this information we infer the most probable cause of the variations. Table 1 summarizes the travel time data for all paths for which 9 or more observations are available. For each path a Student's *t* test has been used to evaluate the hypothesis that the mean travel time (after station corrections have been applied) is the value given by the curve in Fig. 1 and that deviations from this curve can be attributed to random measuring errors. Those ray paths for which the hypothesis could be rejected at the 99.5% confidence level are indicated in Table 1. Fig. 3 shows histograms of the residual distribution for these anomalous paths. For observations at distances beyond 70°, 16 paths (out of 34 tested) showed significant variations from the average curve, whereas for smaller distances, only 3 anomalous paths (out of 22) were found. This strongly suggests that most of the scatter originates in the deep mantle (depth > 2,000 km). The possibility of the variations occurring at a shallower depth

quakes. The difference between the curves in Fig. 1 results from differences in the geographic regions sampled. Possible causes of a regional dependence of this nature are velocity variations in the upper mantle in the source or receiver regions or in the lower mantle, and mislocation of the events (caused by uneven station distribution, and so on). Event mislocation and structure in the receiver regions can be ruled out because they would be expected to produce similar effects at all epicentral distances. Although the observed variations are most striking beyond 85°, we shall show that they are much smaller at distances less than 70°. It is conceivable that structure in the source regions could produce a distance dependent regional variation of this kind, if the velocity anomalies were systematically located relative to the earthquake hypocentres (as indeed they are beneath island arcs). In that case the variations would have to be localized in a very small region beneath the hypocentres, because a 10° distance interval maps into about a 5° difference in angle at the focus. Even if the anomalous regions are as deep as 1,000 km, the velocity change must occur over a horizontal distance of only 50 km or so. This possibility may be ruled out because all the earthquakes in each source region yield a similar pattern of travel time residuals, even though the epicentre locations in each region are typically distributed over > 200 km. Velocity

Fig. 3 Histograms of travel time residuals (relative to curve of Fig. 1 with station corrections applied) for different ray paths through the mantle. Identification numbers correspond to those in Table 1 and Fig. 4. *N* is the number of observations.

Table 1 Travel Time Statistics for Mantle P Wave Paths

Identification No.	N	$\bar{x}$	s	t	$t_{99.5}$	Path
(a) $85° < \Delta < 100°$						
1–1*	17	0.46	0.43	4.41	3.25	Japan—USA
1–2	12	−0.11	0.56	−2.15	3.50	Bonin and Marianas Arc—USA
1–3*	15	−0.76	0.48	−6.13	3.33	Tonga Arc—Alaska
1–4*	90	0.23	0.50	4.37	2.89	Tonga Arc—Western North America
1–5*	29	−0.34	0.57	−3.21	3.05	Argentina—Western North America
1–6*	40	0.37	0.70	3.34	2.97	South America—Northwestern Europe
1–7*	84	0.38	0.79	4.40	2.89	South America—Southern Europe
1–8	11	0.06	0.56	0.36	3.58	South America—Southern Africa
1–9*	13	−1.09	0.91	−4.31	3.43	Kuril Arc—Spain, Morocco and Algeria
1–10	16	−0.36	0.58	−2.48	3.29	Bonin Arc—Europe
1–11	42	−0.19	0.65	−1.90	2.97	Indonesia and Philippine Is.—Central and Northern Europe
1–12	14	0.16	0.48	1.25	3.37	Indonesia and Philippine Is.—Middle East and Balkans
1–13	13	0.47	0.96	1.77	3.43	Indonesia and Philippine Is.—Central and Southern Africa
1–14	10	−0.12	0.56	−0.68	3.69	Tonga Arc—Siberia and China
1–15	9	−0.24	0.28	−2.57	3.83	Indonesia—Alaska
1–16*	56	0.34	0.61	4.17	2.92	Solomon Is.—Western USA
1–17	29	0.04	0.33	0.65	3.05	New Hebrides—Western North America
(b) $70° < \Delta < 85°$						
2–1	57	−0.12	0.45	−2.02	2.92	Japan—USA
2–2*	12	−0.51	0.36	−4.90	3.45	Japan—Southwestern USA
2–3*	34	−0.38	0.37	−5.99	3.01	Bonin Arc—Western USA
2–4*	122	0.16	0.40	4.38	2.86	Tonga Arc—Western North America
2–5*	27	−0.27	0.39	−3.60	3.07	Kuril Arc—Eastern North America
2–6*	76	−0.19	0.45	−3.68	2.90	Argentina and Bolivia—Central and Western USA
2–7*	30	0.25	0.44	3.11	3.04	South America—Spain and Northern Africa
2–8	20	−0.09	0.45	−0.89	3.17	South America—Central and Southern Africa
2–9*	58	0.19	0.43	3.36	2.92	Kuril Arc—Western Europe
2–10*	69	−0.33	0.52	−5.28	2.91	Japan—Western Europe
2–11	22	0.02	0.36	0.26	3.14	New Hebrides—Western North America
2–12	20	−0.06	0.47	−0.57	3.17	Indonesia and Philippine Is.—Middle East
2–13	30	−0.09	0.52	−0.95	3.04	Bonin and Marianas Arcs—Scandinavia and Western Russia
2–14	23	0.14	0.38	1.77	3.12	Japan and Kuril Arc—Australia
2–15	11	−0.06	0.54	−0.37	3.58	Kuril Arc—Middle East
2–16	12	−0.39	0.56	−2.41	3.50	Indonesia—Antarctica
2–17	10	−0.22	0.25	−2.78	3.69	Marianas Arc—Western USA
2–18	12	−0.22	0.69	−1.10	3.50	Japan—Middle East
(c) $55° < \Delta < 70°$						
3–1*	93	0.23	0.38	5.84	2.89	Kuril Arc—Western USA
3–2	45	0.12	0.40	2.01	2.96	Northern South America—Western USA
3–3	42	0.06	0.49	0.79	2.97	Bolivia and Argentina—Central USA
3–4	93	−0.05	0.54	−0.89	2.89	Kuril Arc and Sea of Japan—Northern and Eastern Europe and Middle East
3–5	30	−0.09	0.41	−1.20	3.03	Indonesia and Philippine Is.—Southwestern Asia
3–6	15	0.18	0.62	1.12	3.33	Japan and Kuril Arc—Melanesia
3–7	12	−0.04	0.41	−0.34	3.43	Tonga Arc—Western Australia
3–8	10	−0.28	0.45	−1.97	3.58	Japan and Kuril Arc—Australia
3–9	9	−0.19	0.55	−1.04	3.69	New Hebrides—China and Siberia
3–10	8	0.13	0.78	0.47	4.03	Solomon Is.—Japan
3–11	15	0.26	0.47	2.14	3.29	Tonga Arc—Antarctica
3–12	9	0.22	0.58	1.14	3.69	Indonesia—New Zealand
3–13	10	0.15	0.59	0.80	3.58	Indonesia—Antarctica
(d) $40° < \Delta < 55°$						
4–1*	23	0.41	0.48	4.10	3.12	Kuril Arc—Northwestern North America
4–2	44	−0.18	0.48	−2.49	2.97	Northern South America—USA
4–3	15	0.35	0.41	3.31	3.33	Kuril Arc—Northern Europe
4–4	34	0.16	0.43	2.17	3.01	Japan—Southwestern Asia
4–5	17	−0.25	0.51	−2.02	3.22	Indonesia—India and Pakistan
4–6*	17	0.82	0.56	6.03	3.25	Japan—Alaska
4–7	13	−0.51	0.65	−2.82	3.37	Indonesia—Japan and Korea
4–8	40	0.02	0.55	0.23	2.97	Indonesia—Southeastern Australia and Tasmania
4–9	20	−0.06	0.58	−0.46	3.15	Solomon Is.—Japan, Korea, and Eastern China

N=Number of observations.

$\bar{x}$=Mean travel time residual after station correction (s).

s=Standard deviation of residuals (s).

$$t = \frac{\bar{x}}{s/\sqrt{N}}$$

$t_{99.5}$=99.5% confidence limit for $|t|$ if true mean is zero.

* Indicates paths with mean significantly different from zero.
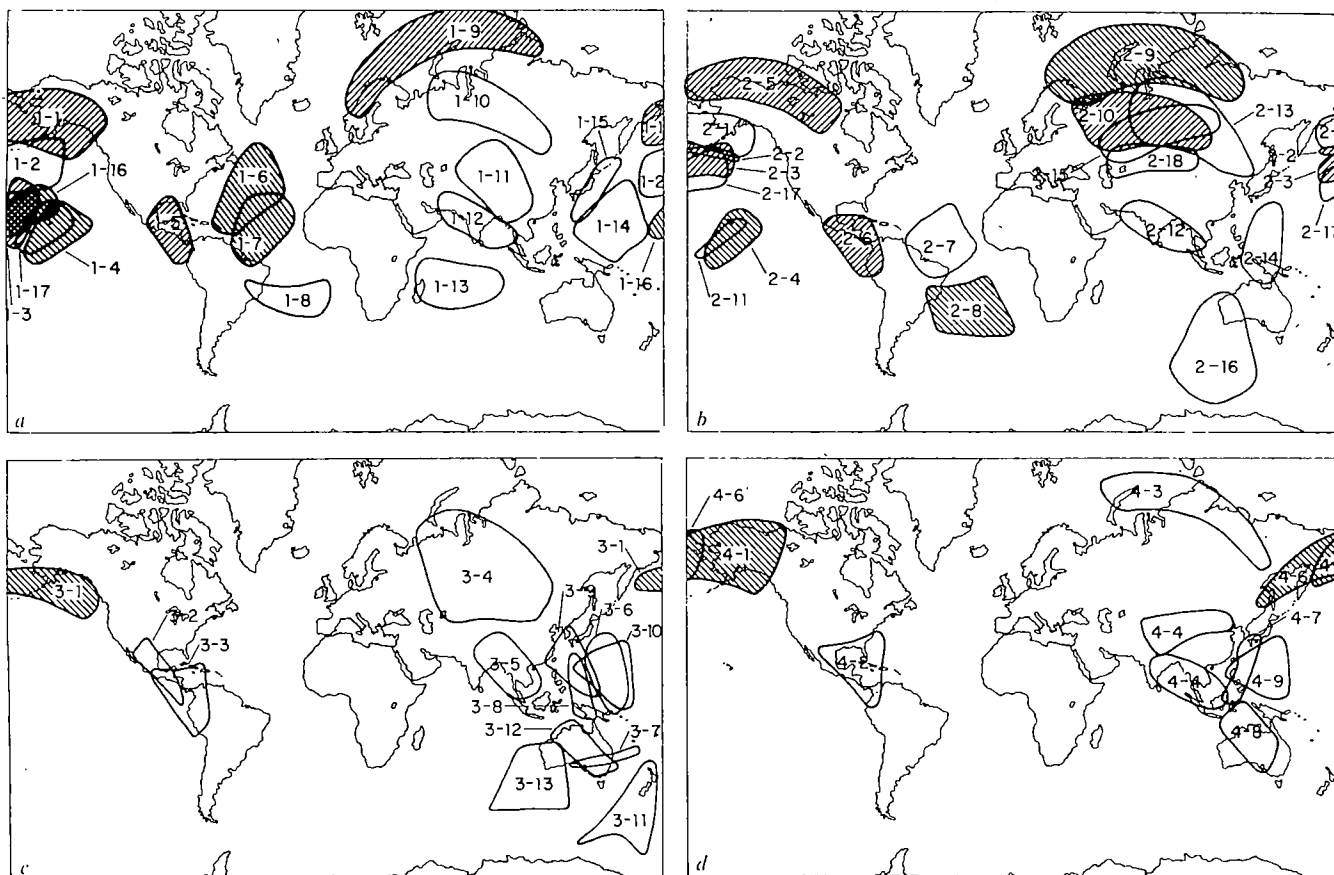
Fig. 4 Regions where paths of observed P waves bottom in the mantle. Cross-hatching indicates regions differing significantly from the mean determined from all data. Other regions tested are outlined. The identification numbers correspond to those in Table 1 and Fig. 3. ▨, Late; ▨, early.

cannot be absolutely disproved, but the velocity distribution in the Earth would have to be such that, given the distribution of earthquakes and seismic stations, all observed waves bottoming at the depth of the heterogeneities happen to be unaffected by them (even though P waves spend about 25% of their travel time traversing the lowest 10% of the ray path), while waves penetrating beneath the heterogeneities are affected. It seems unreasonable to assume such a conspiratorial behaviour on the part of the velocity variations when a much simpler hypothesis is available.

The actual details of the velocity distribution cannot, however, be determined precisely, because rays travel a great distance at approximately the same depth near their turning points. Fig. 4 shows the regions of the lower mantle sampled by the various ray bundles (defined arbitrarily as the central 30° of each path) and indicates which paths correspond to early and late arrivals. These are in most cases probably the regions where the actual velocity anomalies occur. Where regions overlap on the figure, they are generally consistent with each other (for example, regions 1–6 and 1–7, regions 2–2 and 2–3, and regions 4–1 and 4–6). This consistency is encouraging, in that it supports our argument that the travel time anomalies originate in the deep mantle and are not the result of some other type of systematic error. An apparent inconsistency exists between regions 1–3 and 1–16, but this is not surprising because of the uncertainty as to exactly where the travel time anomalies actually originate. The rays following path 1–3 also pass through regions 2–2 and 2–3 further to the north, and it is likely that the travel time anomaly actually originates there. Another interesting feature of Fig. 4 is a correlation between the anomalies in the two greatest distance ranges (for example, regions 1–7 and 2–7, regions 1–4 and 2–4, and regions 1–5 and 2–6), suggesting that the structure in the deep mantle has a spatial "coherence" of at least a few hundred km vertically.

The mean travel times in Table 1 show a variation of about 1.5 s for rays bottoming below 2,600 km, and about 0.6 s for rays bottoming between 2,000 and 2,600 km. These numbers are somewhat uncertain, but it is likely that the true travel times vary by at least 1 s. The amount by which the actual velocity in the mantle varies depends on the size of the regions within which the variations occur. The data of Fig. 4 suggest that the size of some of the anomalies, at least, is about 1,000 km or less, in which case the velocity must vary by at least 1%. This is a lower bound both because we have probably over-estimated the scale of the inhomogeneities and because we are measuring averages of the velocity in rather large regions and some cancellation of the effects of positive and negative velocity anomalies is likely. Combined interpretation of travel time and $dT/d\Delta$ measurements can probably improve the resolution of structural details.

Might the deep mantle variations be related in some way to the convection plumes hypothesized by Wilson[10] and Morgan[11] to exist in the deep mantle? To answer this the region of the Hawaiian Islands provides the best data, and here they indeed indicate a pronounced lateral variation, the velocities being high to the northwest of Hawaii (regions 2–2, 2–3, and probably 1–3) and low in the vicinity of the islands (regions 1–4, 2–4, and 1–6). Interestingly, the $dT/d\Delta$ data presented by Davies and Sheppard[4] also indicate a horizontal velocity contrast of this sort in the vicinity of Hawaii. Unfortunately, no other proposed plumes are well sampled by our data. Region 1–13 includes the Mascarene Islands, but the data here are highly scattered, and no conclusion can be drawn. Regions 1–5 and 2–6, both with apparently high velocities, are located slightly to the northeast of the Galapagos Islands, so it is not clear what relation, if any, this velocity anomaly may bear to a possible plume. If travel time data for rays passing through more proposed plume regions can be obtained, they may

provide valuable evidence relevant to the Wilson–Morgan hypothesis.

Except, perhaps, for the Hawaiian Islands, no geological or tectonic features show an obvious correlation with the inferred deep mantle velocity anomalies. At shallower depths, however, this is not the case; regions 3–1, 4–1, and 4–6, all seeming to have low velocities, lie beneath the Kurile and Aleutian Island arcs. The only other island arc adequately sampled at these depths lies beneath Middle America (region 4–2) and is associated with early arrivals (though they are not significant at the 99.5% confidence level). The data thus suggest that low velocities may be characteristic of island arcs at depths greater than 1,000 km.

The data considered here do not support any correlation between velocity variations below 2,000 km and global gravity anomalies or geoid heights. At shallower depths such a correlation does exist, but it is merely another manifestation of the low velocities beneath the Kurile and Aleutian Islands, because the concave sides of island arcs are generally the sites of prominent positive free air gravity anomalies.

It is not possible to make a direct comparison between these results and those of Alexander and Phinney[5]. The region of the North Atlantic found by them to be anomalous is further east than the corresponding region sampled by our data. Further, travel time measurements such as ours provide a measure of the average velocity in a region, whereas the behaviour of core diffracted waves depends on features such as the velocity gradient in the lower mantle. Further studies of variations in the "visibility" within the core shadow would be a useful complement to travel time and $dT/d\Delta$ studies of the lower mantle.

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Evidence for an Advanced Plio-Pleistocene Hominid from East Rudolf, Kenya

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Four specimens collected last year from East Rudolf are provisionally attributed to the genus *Homo*. One, a cranium KNM-ER 1470, is probably 2.9 million years old.

PRELIMINARY descriptions are presented of four specimens collected from East Rudolf during 1972. Most of the collection recovered during this field season has been reported recently in *Nature*[1]; the specimens described here are sufficiently important to be considered separately and in more detail. The collections of fossil hominids recovered from East Rudolf during earlier field seasons and detailed descriptions of some of these specimens have been published previously[2-5].

The specimens described here are: (1) a cranium, KNM-ER 1470; (2) a right femur, KNM-ER 1472; (3) a proximal fragment of a second right femur, KNM-ER 1475; and (4) an associated left femur, distal and proximal fragments of a left tibia, and a distal left fibula, KNM-ER 1481. They were all recovered from area 131 (see Fig. 1) and from deposits below the KBS Tuff which has been securely dated at 2.6 m.y.[6].

Area 131 consists of approximately 30 km² of fluviatile and lacustrine sediments. The sediments are well exposed and show no evidence of significant tectonic disturbance; there is a slight westward dip of less than 3°. Several prominent marker horizons provide reference levels and have permitted physical correlation of stratigraphical units between area 131 and other areas in the East Rudolf locality.

Several tuffs occur in the vicinity of area 131. The lowest of these is the Tulu-Bor Tuff which is not exposed in the area itself but does outcrop nearby in several stream beds. Above this horizon, in a composite section, there is some 60 m of sediment capped by the prominent KBS Tuff. This latter tuff has been mapped into areas 108 and 105 (also shown in Fig. 1) from where samples have been obtained for K/Ar dates. An account of the geology is given by Vondra and Bowen[7]. A section showing the vertical position of these four hominids in relation to the KBS Tuff is given in Fig. 2.

At present, analysis of samples collected for dating from the KBS Tuff in area 131 has proved inconclusive because of the apparent alteration of the sanidine felspars. This was not seen in the 105/108 samples from the same horizon which provided the date of 2.61 m.y. and there is no reason to suspect the validity of that date (personal communication from J. A. Miller).

Detailed palaeomagnetic investigation of the sedimentary units is being undertaken by Dr A. Brock (University of Nairobi). Systematic sampling closely spaced in the section has identified both the Mammoth and Kaena events in area 105 between the Tulu-Bor and KBS Tuffs, a result which supports the 2.61 m.y. date on the latter. The mapping of several

horizons has established a physical correlation between areas 105 and 131. During the 1973 season, the area 131 succession will be sampled in detail in an attempt to confirm this correlation. Available evidence points to a probable date of 2.9 m.y. for the cranium KNM-ER 1470, and between 2.6 and 2.9 m.y. for the other specimens reported here.
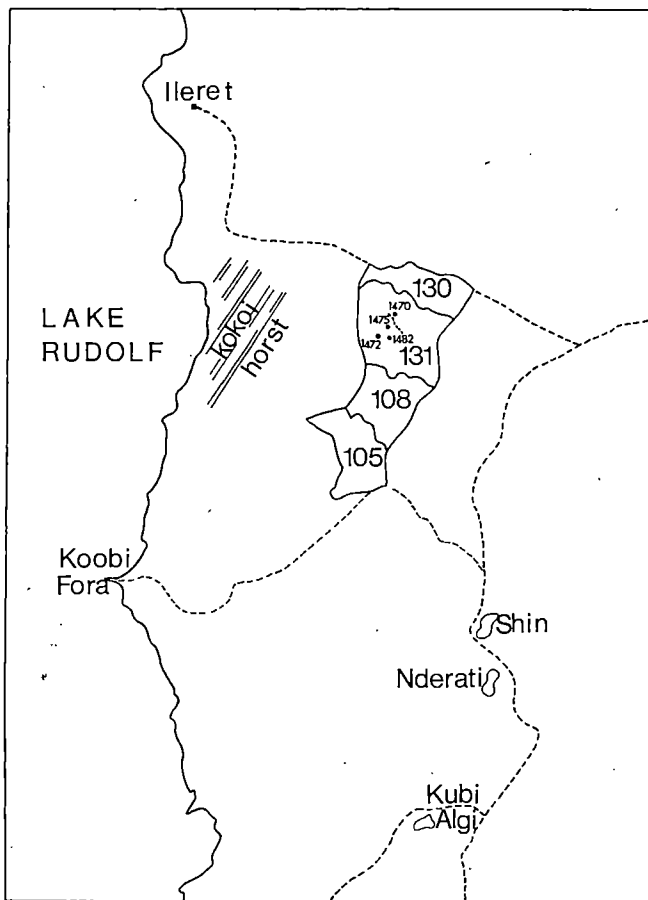
Fig. 1 Map showing sites of discovery of fossil hominids KNM-ER 1470, 1472, 1475 and 1481 in the East Rudolf locality. Succession shown in Fig. 2 was taken from the position indicated by the dotted line.

Collections of vertebrate fossils recovered from below the KBS Tuff in areas 105, 108 and 131 all show the same stage of evolutionary development and this evidence supports the indicated age for this phase of deposition at East Rudolf. Maglio[8] has discussed the fossil assemblages following detailed studies of field collections from various horizons.

The cranium (KNM-ER 1470) and the postcranial remains (KNM-ER 1472, 1475 and 1481) were all recovered as a result of surface discovery. The unrolled condition of the specimens and the nature of the sites rules out the possibility of secondary deposition—there is no doubt in the minds of the geologists that the provenance is as reported. All the specimens are heavily mineralized and the adhering matrix is similar to the matrix seen on other fossils from the same sites. In due course, microscopic examination of thin sections of matrix taken from the site and on the fossils might add further evidence.

Cranium KNM-ER 1470

Cranium KNM-ER 1470 was discovered by Mr Bernard Ngeneo, a Kenyan, who noticed a large number of bone fragments washing down a steep slope on one side of a gully.

Careful examination showed that these fragments included pieces of a hominid cranium. An area of approximately 20 m × 20 m was subsequently screened and more than 150 fragments were recovered.

The skull is not fully reconstructed. Many small fragments remain to be included and it may be some time before the task is completed. At present the cranial vault is almost complete and there are good joins between the pieces. The face is less complete and although there are good contacts joining the maxilla through the face to the calvaria, many pieces are still missing. The orientation of the face is somewhat uncertain because of distortion of the frontal base by several small, matrix filled cracks. The basicranium shows the most damage and is the least complete region.
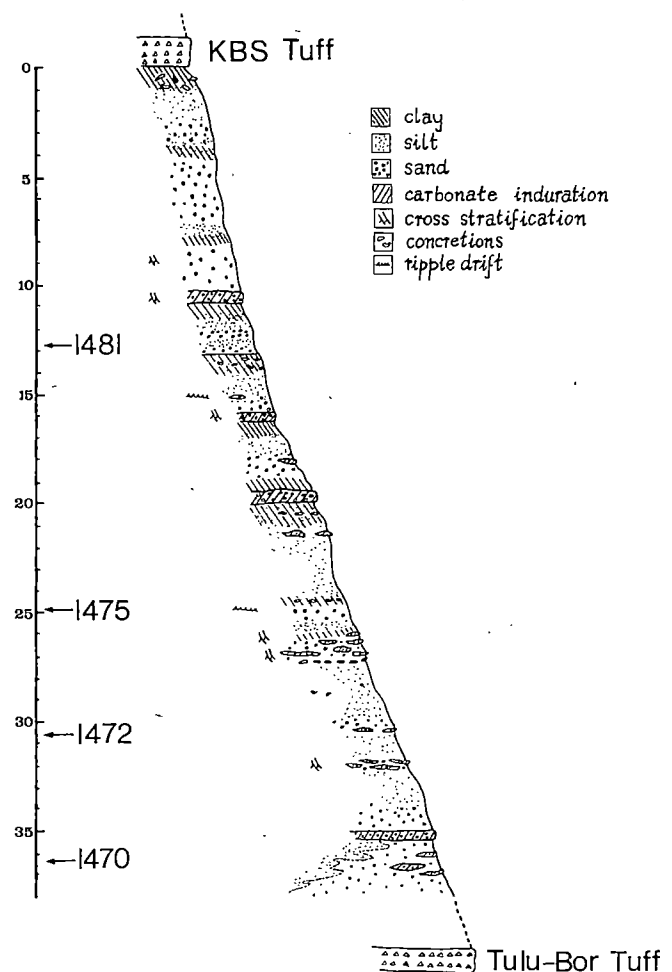
Fig. 2 Stratigraphical succession of the sediments in area 131 and the vertical relationships of the fossil hominids KNM-ER 1470, 1472, 1475 and 1481 to the KBS Tuff. Dotted line shown in Fig. 1 marks the position at which the section was taken.

The cranium (see Fig. 3) shows many features of interest. The supraorbital tori are weakly developed with no continuous supratoral sulcus. The postorbital waisting is moderate and there is no evidence of either marked temporal lines or a temporal keel. The vault is domed with steeply sloping sides and parietal eminences. The glenoid fossae and external auditory meati are positioned well forward by comparison with *Australopithecus*. The occipital area is incomplete but there is no indication of a nuchal crest or other powerful muscle attachments.

In view of the completeness of the calvaria, it has been pos-

Fig. 3 Cranium KNM-ER 1470. *a*, Facial aspect; *b*, lateral aspect; *c*, posterior aspect; *d*, superior aspect.

sible to prepare in modelling clay an endocranial impression which has been used to obtain minimum estimates for the endocranial volume. Six measurements of the endocast by water displacement were made by Dr A. Walker (University of Nairobi), and gave a mean value of 810 cm³. Further work on this will be undertaken but it seems certain that a volume of greater than 800 cm³ for KNM-ER 1470 can be expected.

The palate is shallow, broad and short with a nearly straight labial border that is reminiscent of the large *Australopithecus*. The great width in relationship to the length of the palate does contrast markedly, however, with known australopithecine material. The molars and premolar crowns are not preserved, but the remaining roots and alveoli suggest some mesiodistal compression. The large alveoli of the anterior teeth suggest the presence of substantial canines and incisors.

Femur KNM-ER 1472

KNM-ER 1472, a right femur, was discovered as a number of fragments by Dr J. Harris. It shows some features that are also seen in the better preserved left femur, KNM-ER 1481, but other features, such as the apparently very straight shaft and

the bony process on the anterior aspect of the greater trochanter, require further evaluation.

Femoral Fragment KNM-ER 1475

The proximal fragment of femur, KNM-ER 1475, was discovered by Mr Kamoya Kimeu. Its condition is such that a final taxonomic identification will be difficult and it is therefore included only tentatively in this report. This fragment shows some features such as a short, more nearly cylindrical neck, which are not seen in the femurs of *Australopithecus*.

Associated Skeleton KNM-ER 1481

A complete left femur, KNM-ER 1481, associated with both ends of a left tibia and the distal end of a left fibula were also discovered by Dr J. Harris.

The femur (see Fig. 4) is characterized by a very slender shaft with relatively large epiphyses. The head of the femur is large and set on a robust cylindrical neck which takes off from

the shaft at a more obtuse angle than in known *Australopithecus* femurs. There is a marked insertion for gluteus maximus and the proximal region of the shaft is slightly flattened antero-posteriorly. The femoro-condylar angle is within the range of *Homo sapiens*. When the femur is compared with a restricted sample of modern African bones, there are marked similarities in those morphological features that are widely considered characteristic of modern *H. sapiens*. The fragments of tibia and fibula also resemble *H. sapiens* and no features call for specific comment at this preliminary stage of study.

Homo or *Australopithecus* ?

The taxonomic status of the material is not absolutely clear, and detailed comparative studies which should help to clarify

(ref. 10). The Olduvai material is only known from deposits that are stratigraphically above a basalt dated at 1.96 m.y. (ref. 11). At present therefore there does not seem to be any compelling reason for attributing to this species the earlier, larger brained, cranium from East Rudolf.

The 1470 cranium is quite distinctive from *H. erectus* which is not certainly known from deposits of equivalent Pleistocene age. It could be argued that the new material represents an early form of *H. erectus*, but at present there is insufficient evidence to justify this assertion.

There is no direct association of the cranial and postcranial parts at present, and until such evidence becomes available, the femora and fragment of tibia and fibula are only provisionally assigned to the same species as the cranium, KNM-ER 1470. Differences from the distinctive *Australopithecus* postcranial elements seem to support this inferred association.

Fig. 4   Left femur KNM-ER 1481. *a*, Posterior aspect; *b*, anterior aspect.
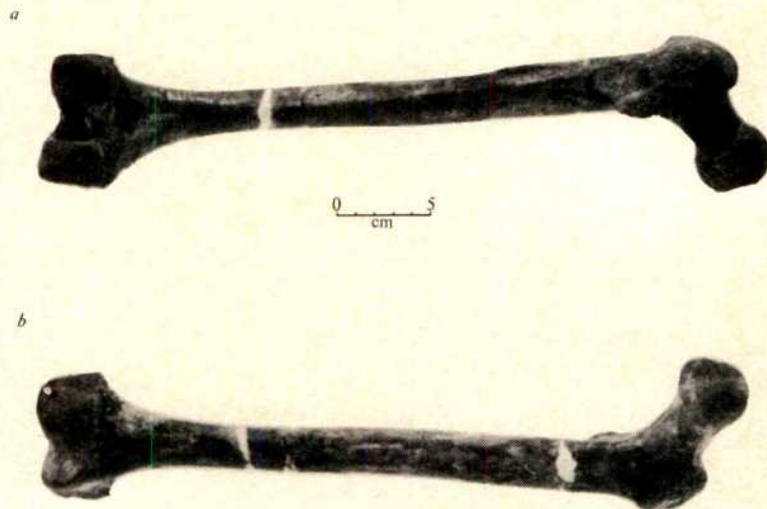
this problem have yet to be concluded. The endocranial capacity and the morphology of the calvaria of KNM-ER 1470 are characters that suggest inclusion within the genus *Homo*, but the maxilla and facial region are unlike those of any known form of hominid. Only the flat fronted wide palate is suggestive of *Australopithecus*, but its extreme shortening and its shallow nature cannot be matched in existing collections representing this genus. The postcranial elements cannot be readily distinguished from *H. sapiens* if one considers the range of variation known for this species.

The East Rudolf area has provided evidence of the robust, specialized form of *Australopithecus* from levels which span close to 2 m.y. (2.8 m.y.–1.0 m.y.)[1]; throughout this period the morphology of this hominid is distinctive in both cranial and postcranial elements. The cranial capacity of the robust australopithecine from Olduvai Gorge, *A. boisei*, has been estimated for OH 5 to be 530 cm³ (ref. 9); this is the same value as that estimated by Holloway for the only specimen in South Africa of *A. robustus* which provides clear evidence of cranial capacity[9]. Holloway has also found the mean cranial capacity of six specimens of the small gracile *A. africanus* from South Africa[10] to be 422 cm³. Thus, to include the 1470 cranium from East Rudolf within the genus *Australopithecus* would require an extraordinary range of variation of endocranial volume for this genus. This seems unacceptable and also other morphological considerations argue strongly against such an attribution.

The Olduvai Gorge has produced evidence of an hominine, *H. habilis*; the estimated endocranial volumes for three specimens referred to this species are 633, 652 and 684 cm³

For the present, I propose that the specimens should be attributed to *Homo* sp. indet. rather than remain in total suspense. There does not seem to be any basis for attribution to *Australopithecus* and to consider a new genus would be, in my mind, both unnecessary and self defeating in the endeavour to understand the origins of man.

I should like to congratulate Mr Ngeneo and Dr Harris for finding these important discoveries. Dr Bernard Wood spent many long hours at the site screening for fragments and assisted my wife, Meave, and Dr Alan Walker in the painstaking reconstruction work. I thank them all. The support of the National Geographic Society, the National Science Foundation, the W. H. Donner Foundation and the National Museum of Kenya is gratefully acknowledged.

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LETTERS TO NATURE

PHYSICAL SCIENCES

Oceanic Observation of New York Bight by ERTS-1

ON August 16, 1972, the multispectral scanner (MSS) aboard the first Earth Resources Technology Satellite (ERTS) obtained images of New York Bight which contain information of oceanographic significance. The images demonstrate the effectiveness of satellite use in observing surface features that indicate variations of water quality.

The MSS measures reflectance of solar energy in four channels with band pass filters that cover visible and near infrared bands from 0.5 to 1.1 μm. Because solar energy penetrates ocean water further for the shorter observed wavelengths, features characteristic of the water mass, such as turbidity, are more predominant in the lower bands; features on or above the sea surface, such as clouds, tend to appear with uniform strength in all channels (Fig. 1). A nearly perfect target at 5 m will reflect 50% of the energy in the lowest band and essentially none in the highest band.

Fig. 2 shows imagery from the band most sensitive to ocean features—MSS-5; MSS-4 is partly obscured with haze induced by atmospheric scatter. The most prevalent oceanic feature in this frame is visibly turbid surface water near the coast. A plume of light-coloured water extends from the New York harbour complex south along the New Jersey coast. The plume, approximately 18 mile long and 7 mile wide, represents the offshore Hudson River effluent. The Hudson River plume is relatively small at this time of year owing to reduction in the outflow of fresh water and is pushed on to the New Jersey coast by the prevailing winds.

Inhomogeneities in the plume indicate the turbulent mixing processes by which plume water is absorbed into ambient Bight water. The relatively sharp eastern boundary of the plume suggests that dispersion processes are not isotropic.

There are features in the Bight apex about 20 mile southeast of the harbour entrance, seemingly manifestations of human activity in the area. A line and a more diffuse circular patch north of the line are seen in this frame. These features are located in the general area used for waste disposal[1].
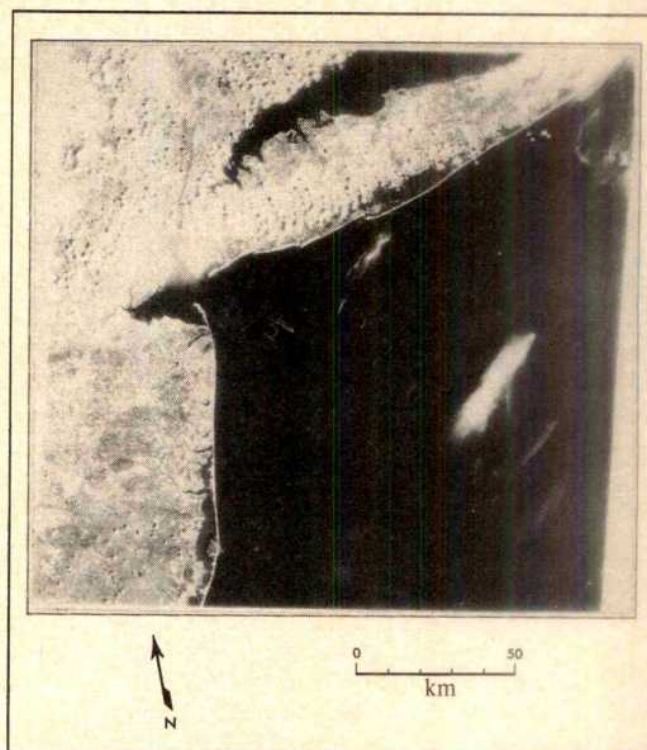
The line resulted from the disposal of waste acid. Less distinct portions of the line may be the residue of an earlier dump, at least 12 h before; dispersion has evidently been slow. Even though wind mixing was low for that day it is apparent that dumping of this magnitude will usually produce a persistent surface feature. Subsequent ERTS images all show dump residues.

The diffuse circular patch to the north of the waste acid dump is close to the sewer sludge dump site. Surface vestige of a sewer sludge dump is much less noticeable than waste acid; only a grey-brown slick remains. Initial low intensity of reflected light makes the character of the surface patch less discernible.

It seems likely that satellites with sensors optimized to view the ocean in visible and infrared wavelengths, supplying synoptic data over large areas, will materially aid management of the coastal zone on a broad scale.

Fig. 1   Theoretical calculation of the proportion of solar energy penetrating the sea surface that reaches a given depth for each of the four channels of the ERTS MSS. Calculations used the attenuation coefficient for pure water. This provides a conservative estimate because for the cleanest sea water α is much larger.

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Organic Mercury Compounds in Coastal Waters

ORGANIC mercury compounds have been demonstrated in biological material[1-3] and the pioneering work of Jensen and Jernelov[4-6] and Wood, Rosen and Kennedy[7] has demonstrated that these organic mercury compounds can be synthesized by microorganisms in fresh water sediments. Their studies strongly suggest that organic compounds of mercury may be present in natural waters, although there is little experimental evidence for the existence of organic forms of Hg in either fresh or marine water. The role of mercury and its ultimate fate in fresh or marine environments will depend on its chemical and physical form. Thus, a meaningful assessment of the effects of toxic or latently toxic metals, such as mercury, on the biosphere requires identification and differentiation of the various chemical species of the metal in the environment. Here we present experimental data indicating the presence of organic forms of mercury in river water and in coastal seawater, and we hope to encourage further study of the role of mercury in natural waters.

We have determined total and inorganic mercury in coastal waters and adjacent river waters in the vicinity of Long Island Sound. The mercury determinations were made on two different sets of 100 ml. aliquots of natural water. Both sets of samples were collected in glass bottles and acidified to pH 1.0 with redistilled concentrated nitric acid. The first set of samples was analysed directly, and gave the concentration of inorganic mercury. The second set of samples was photo-oxidized for at least 24 h using a modification of the ultraviolet-irradiation method[8] for the destruction of dissolved organic carbon in natural waters[9]. These aliquots were then analysed, and this measurement gives the total amount of mercury present. The total mercury minus inorganic equals the mercury associated organically.

Mercury was measured by a modification of the standard flameless atomic absorption technique[10]. That is, a simple but effective non-contaminating method for concentrating Hg before its passage through the gas cell was developed and employed for these determinations. After reduction Hg is trapped while purging (N_2 gas) and concentrated on a packed column ('Chromosorb' WHP; 80/100 mesh, 1.5% OV-17 and 1.95% QF-1) immersed in a liquid nitrogen bath[11]. When purging is complete, the column is removed from the cold trap, heated and the gas phase absorption (2537 Å) of the eluted Hg is measured using a 'Coleman' Hg analyser (MAS-50). A detection limit of 0.0017 μg Hg l.$^{-1}$ is obtained using a ×20 scale expansion on the recorder.

Table 1 Mercury Fractions in Long Island Sound Waters

Location	Date of collection	Salinity %oo	Mercury concentration (μg l.$^{-1}$) Total*	Inorganic†	Organic
Connecticut River	August 21, 1972	0.09	0.045	0.021	0.024
Avery Point Dock Water	September 26, 1972	29.7	0.067	0.025	0.042
Fishers Island Sound	August 17, 1972	30.1	0.078	0.028	0.050
Race, Long Island Sound	October 13, 1972	30.3	0.047	0.033	0.014

* Amount of Hg measured in the organic free (photo-oxidized) acidified water samples.

† Amount of Hg measured in the raw acidified water samples.

The precision of analysis for Hg is 15% based on repeats of a standard sample (concentration at 0.025 μg Hg l.$^{-1}$) and reported as a coefficient of variation. The samples were not filtered and the concentrations reported include the contribution of acid leachable mercury associated with particulate material. Some of this mercury solubilized by the acid treatment may be in an organically associated form, and this quantity will appear in our total mercury measurements. Burton and Leatherland[12] found the acid leachable portion to be not greater than 10% of the total measurable mercury in the dissolved form. As yet, we have not analysed particulate matter for its mercury content or fractions.

The contentrations of inorganic, organic and total mercury found in this study are given in Table 1. It is most significant

Table 2 Summary of Mercury Determinations in Seawater

Ocean region	Date of report	Mercury concentration	Experimental method	Reference
North Sea	1934	0.03 μg l.$^{-1}$	Electrochemical following co-precipitation with CuS	(13)
Ramapo Deep—off Japan	1961	0.08–0.25 μg l.$^{-1}$	Spectrophotometry after dithizone extraction	(14)
British Coastal Waters	1971	0.011–0.021 μg l.$^{-1}$	Spectrophotometry after anion exchange concentration	(12) *
North Atlantic	1971	0.003–0.020 μg l.$^{-1}$	As reference 12	(15)
Canadian Continental Shelf	1972	0.058–0.071 μg/kg	Gas phase atomic absorption spectrophotometry	(16) †
Pacific Ocean: off Coast of Mexico	1972		Thermal neutron activation after co-precipitation with CuS	(17)
60 km		0.022–0.153 μg/kg		
150 km		0.012–0.025 μg/kg		
Greenland Sea	1972	0.016–0.364 μg l.$^{-1}$	Gas phase atomic absorption spectrometry after Au amalgamation	(18)

* British river waters were found to contain 0.009–0.010 μg Hg l.$^{-1}$.

† Along a Nova Scotian estuary, 0.046–0.201 μg Hg kg^{-1} was measured.

that as much as 50–60% of the mercury present in these waters (river and coastal seawater) may exist either as organic compounds or in association with the organic matter (Table 1). This determination of mercury associated with organic material is from an indirect gross measurement of the contribution of mercury liberated from the total organic background. At present, we have no idea of how Hg is bound in the chemical species making up the organic mercury portion.

Previous investigations of mercury in the marine environment have been concerned principally with total mercury concentrations. The reported amounts for Hg in seawater vary from 0.003 to 0.364 μg l.$^{-1}$ (Table 2). Our data are certainly within this broad range, but much of the mercury may be present in organically associated forms that are not always reactive or measurable by the commonly employed techniques. Apart from normal analytical consideration, it is difficult therefore to evaluate and comment on available Hg data in natural waters. This analytical anomaly will vary with technique and even within a study if the organic background is changing.

The work tabulated in Table 2 and our determinations suggest that regional differences exist for the mercury concentrations in the coastal marine environment. It would appear, for example, that concentrations of Hg reported for British coastal waters are significantly lower than those found in Long Island Sound or the Canadian Shelf waters. As noted, however, there are still uncertainties about the types and amounts of the various mercury species present in marine waters and the fraction being measured. This information will be required to determine more accurately the mercury distribution in the oceans and to elucidate the pathways and interactions of mercury in the estuarine and marine environment. Every effort should be made to develop methods capable of differentiating the various chemical forms of mercury in natural waters.

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Fine Structure in the X-ray Emission Spectrum of N₂, Compared with Electron Spectroscopy

X-RAY emission spectroscopy has considerable potential in studying the valence electron structure of matter, and has been used to examine the electronic band structure of solids. To a much lesser extent it has been applied to the study of molecular orbitals in free molecules, but owing to lack of resolution in the experimental spectra it is difficult to discern very well the different valence orbitals in a molecule. These orbitals have instead been observed and studied in great detail by other techniques, among which electron spectroscopy (ESCA) has been successful in elucidating both valence electron orbitals and core electron orbitals[1,2]. If X-ray transitions involving molecular valence electrons could conveniently be examined with a resolution of 1 eV or better there should be many applications for these types of study. We have constructed an apparatus for this purpose in which the X-ray emission spectra from gaseous samples are excited by electron impact and analysed in a grazing incidence grating spectrometer at a resolving power of 3,000[3,4]. This corresponds to ≈0.1 eV for the characteristic X-radiation of the second period elements. We show here that such high resolution in the X-ray spectrum reveals the molecular orbital structure and molecular states in sufficient detail to allow direct comparisons with molecular ESCA spectra and lets us observe fine structure due to molecular vibration in an X-ray line. Dipole selection rules control the X-ray transitions and serve as a guide in the assignment of the different valence orbitals of the molecule.

We used the nitrogen molecule in our investigation. The N₂ emission spectrum was recorded in 1st, 2nd, 3rd and higher orders on 'Kodak SWR' plates. In some of the exposures the Mo M$_\zeta$ line was also recorded as an energy reference. The nitrogen X-ray emission spectrum is shown in Fig. 1 together with the electron spectrum excited with both AlK$_\alpha$ and HeI radiation. From the value for the Mo M$_\zeta$ line (192.55 ± 0.05 eV) given in ref. 5 the N₂ lines were determined using the dispersion of the instrument. The energies thus established are presented in Table 1.

Table 1 Energies and Assignments of the Lines in the X-ray Spectrum of N₂

	Energy X-ray	ESCA[1,2]	Relative energy X-ray	ESCA[1,2]	Assignment
1	400.81	400.8*			N1s←1π$_g$
2	400.27				Transitions in
3	399.74				doubly ionized
4	399.04				or singly
5	397.14				ionized, excited N₂
6	394.40	394.3	0.00	0.00	N1s←3σ$_g$(X²Σ$_g$⁺)
7	394.17		−0.23	−0.26	
8	393.34†	393.2	−1.06	−1.12	N1s←1π$_u$(A²Π$_u$)
9	391.33	391.1	−3.07	−3.18	N1s←2σ$_u$(B²Σ$_u$⁺)
10	384.5±0.5	385.0	−8.9	−9.7‡	N1s←(C²Σ$_u$⁺)
11	381.3±0.5	381.3	−13.1	−13.0	
12	378.1±0.5	377.9	−16.3	−16.4	
13	372.1±0.5	372.6	−22.3	−21.8	N1s←2σ$_g$(²Σ$_g$⁺)

Energies are expressed in eV, and the energies relative to the 3σ$_g$ line are generally determined with an accuracy of ±0.10 eV or better.
* From ref. 7.
† Refers to the line of highest energy in the band.
‡ From refs. 1 and 6.

The ground state configuration of N₂ is 1σ$_g$²1σ$_u$² (N1s) 2σ$_g$²2σ$_u$²1π$_u$⁴3σ$_g$²; ¹Σ$_g$⁺ with 1π$_g$ orbital as the first empty valence orbital. Fig. 1 and Table 1 show that the X-ray transitions involving the valence orbitals can be identified from a direct comparison between ESCA results and the present ones. The strongest lines (numbers 6, 7, 8, 9 in Fig. 1) are shown with higher resolution in the densitometer curve of the third order spectrum in Fig. 2. These lines correspond to the transitions
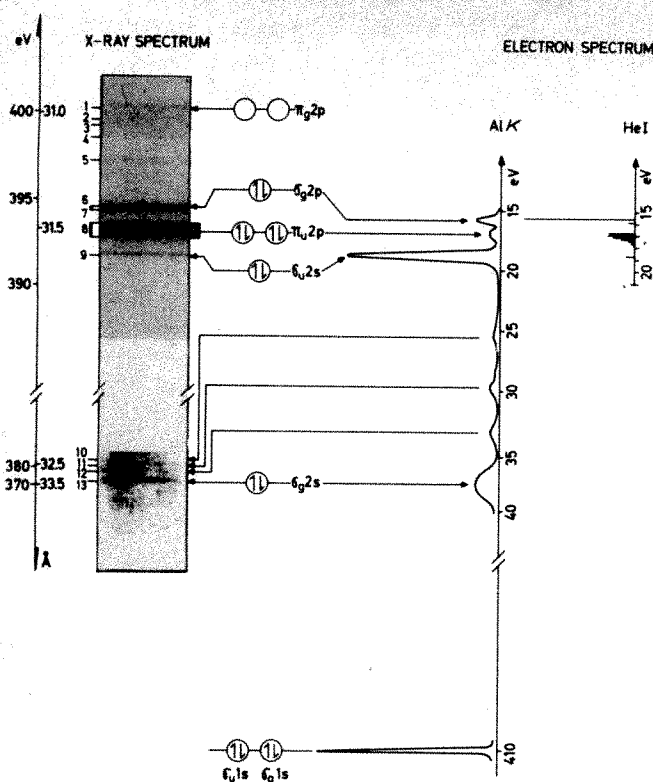
Fig. 1 The X-ray spectrum of N_2 together with the electron spectra excited with the AlK_α and HeI radiations. In the X-ray spectrum the energy region 370–385 eV is shown with a compressed energy scale as compared to the 390–400 eV region.

$N1s \leftarrow 3\sigma_g$, $1\pi_u$ and $2\sigma_u$ and it is obvious from Fig. 2 that the first two of them exhibit fine structure. The $3\sigma_g$ line consists of a strong line with a weaker component at 0.23 eV lower energy, while the $1\pi_u$ line is composed of a progression of lines with an average spacing of 0.20 eV. The spacings between the lines are in excellent agreement with the vibrational splittings in the HeI electron spectrum. We conclude therefore that this fine structure in the X-ray lines can be ascribed to vibrational splittings as has been presented elsewhere (unpublished manuscript). To our knowledge such fine structure within X-ray emission lines has not been observed before.

The profile of the $3\sigma_g$ line confirms that it is a slightly bonding or nearly nonbonding orbital, while the wide envelope of the $1\pi_u$ line agrees with its strongly bonding character. The $2\sigma_u$ line is narrow as can be expected, as this orbital is nominally antibonding. These X-ray lines derive their intensities from the N2p population of the corresponding valence orbitals whereas in the electron spectra both s and p populations contribute, although with different photoelectric cross sections. The $N1s \leftarrow 2\sigma_g$ transition can be seen in Fig. 1 as a broad line (No. 13). The $2\sigma_g$ orbital is considerably broadened (≈ 3 eV) as can also be seen in the electron spectrum. This orbital has about the same N2p character as the $2\sigma_u$ orbital and one would therefore expect almost equal intensity for the X-ray transitions leading to vacancies in these orbitals.

At least three more lines (Nos. 10–12) can be found between the $2\sigma_g$ and $2\sigma_u$ lines. Corresponding lines have been found in ESCA and represent other excited states of the N_2^+ molecule, reached by "shake-up" transitions. Unfortunately the higher excited states of N_2^+ are not well known, but there are doublet states at about 22.0 eV ($D^2\Pi_g$) and 23.6 eV ($C^2\Sigma_u^+$) above the ground states of neutral N_2[6]. An ionization of N_2 in the $2\sigma_u$ orbital leaves the ion in the $B^2\Sigma_u^+$ state which has the same symmetry as the C state and these two states are known to interact[6]. One can therefore expect an X-ray intensity of the $N1s \leftarrow C^2\Sigma_g^+$ transition due to configuration interaction. The ionization potential of N_2 for the vertical transition which

leaves the ion in the $C^2\Sigma_u^+$ state is expected to be 25.3 eV[6]. Because the N1s ionization does not change the internuclear distance appreciably the same energy for the $C^2\Sigma_u^+$ state would be found in the X-ray spectrum. The transition to this state is identified as line No. 10 in our spectrum. Other contributions to the intensity of this line cannot be excluded, however. The remaining low energy satellites (Nos. 11 and 12) may be of similar origin to line No. 10.

Apart from the main X-ray lines and the low energy "shake-up" satellites five high energy satellite lines (Nos. 1–5) have been found. Four of these lines (Nos. 2–5) are quite weak while the one of highest energy (No. 1) is comparable in intensity to the main lines. It is known from X-ray absorption[7], Auger[1,8,9], and ion-electron coincidence[10] experiments that there is a highly excited, auto-ionizing level in N_2, that corresponds to the excitation of an N1s electron into the empty $1\pi_g$ orbital. The energy of this state is 400.8 eV above the ground state in neutral N_2. The X-ray emission process which competes with the auto-ionization, would give rise to a spectral line at this energy as a result of an $N1s \leftarrow 1\pi_g$ "resonance transition" in neutral N_2. The existence of such X-ray phenomena has been pointed out before[1,11,12].
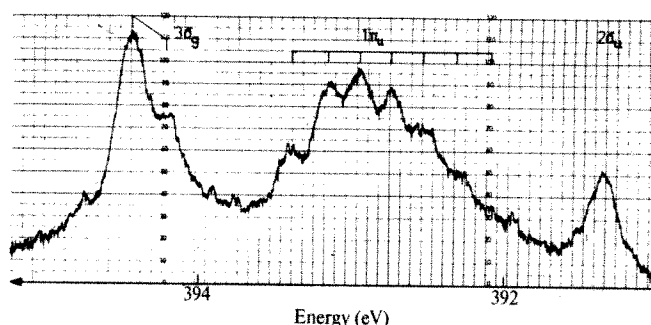
Fig. 2 Densitometer curve of the three main lines in Fig. 1. Fine structure due to molecular vibration is observed in the $3\sigma_g$ and $2\pi_u$ X-ray lines.

The satellite lines 2–5 are probably due to transition in doubly ionized or singly ionized excited molecules. The initial and final states of such transitions can be seen in the shake-up and Auger spectra, respectively, of ESCA. Shake-off begins at about 440 eV in the ESCA spectrum of N_2 (ref. 1) and the final states of the Auger transitions have energies around 43 eV and higher[1]. This gives about the same X-ray transition energies as observed for the satellites 2–5.

Considering the high resolution that can now be obtained in molecular X-ray spectra it appears that this technique will be a useful complement to ESCA. In addition to the N_2 molecule discussed in this paper we have studied argon, CO, CO_2, CS_2 and C_6H_6. Some preliminary results on argon and CO have been published[13,14] and we intend to discuss other aspects of this technique. For example, it is now possible to derive chemical shifts of core electron levels from X-ray and electron spectra, and the localization of valence orbitals on different atomic species within a molecule can be studied in the X-ray spectrum.

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High Strength Glass Fibre-Resin Composites

I have reported that the mean breaking stress of undamaged single fibres of borosilicate glass, tested in tension is consistent at 3.66 kN mm^{-2} over a wide range of fibre diameters, with little scatter[1]. Commercial glass fibre strand, consisting of a large number of fibres aligned in parallel array, fractures at a mean breaking stress of 1.04 kN mm^{-2}; and the value is determined by the individual fibre diameter in the strand. Single fibres taken from such strand have a mean breaking stress of 1.73 kN mm^{-2}. For both strand, and damaged fibres taken from the strand, the scatter in the results is large.

When glass fibres are embedded in a polymeric resin, the resin acts as an adhesive bonding the individual fibres together, and load transference is now possible between the discrete glass fibres. The strength of commercial strand in both epoxide and polyester resins is about 1.7 kN mm^{-2} and again the scatter is large[2].

Many attempts have been made to attain high glass strengths in composites. The methods employed are usually designed to prevent or reduce the amount of damage caused to the surface of the glass fibres during the production of the strand. The most successful way is to coat the glass with the resin during the production of the glass strand[3], before the fibres come into contact with each other. This method, which can produce mean breaking stresses in excess of 2.8 kN mm^{-2}, is difficult to carry out commercially as the fibres are produced at drawing speeds in excess of 3,000 m min^{-1}.

I describe here a new method of achieving high glass strengths in resin composites. Commercial strand contains about 400 fibres each of diameter 0.013 mm, but by changing the drawing speed and the temperature of the fibre production process, strand can be produced over a range of fibre diameters. The fibre used in these experiments was produced in the laboratory with diameters ranging from 0.005 mm to 0.05 mm. The overall cross-sectional area of the strand was kept constant in each case at 0.05 mm^2, the approximate area of commercial strand. This was achieved by varying the number of fibres in the strand from about 20 large fibres to 2,000 very fine fibres in the two extreme cases.

The standard 'Fibreglass' method[4] was used to produce the glass fibre, in which glass is melted in an electrically heated platinum-rhodium crucible. Molten glass is drawn through nozzles in the base of the crucible and is wound onto a revolving drum at high speed.

After production, the strand was embedded in a series of polymeric resins and each strand was tested in tension, at a gauge length of 50 mm, at a strain rate of 25 mm min^{-1}, in an Instron Tensile Testing Machine, until fracture occurred. Forty samples were tested at each fibre diameter.

The results obtained for the mean breaking stress, based on the initial glass cross-sectional area, for three widely differing resin media are shown in Table 1, in which the scatter in the results is shown by the coefficient of variation. The values for the breaking stress of strand with no resin present, for commercial strand, and commercial strand in the three resins are included for comparison.

Table 1 Mean Breaking Stress and Scatter for Glass Fibres Embedded in Various Resins

Type of composite	Fibre diameter μm	Mean breaking stress GN m^{-2}	Coefficient of variation ± %
Strand only	6.10	1.064	15.8
	10.92	0.913	11.0
	12.95	0.899	20.8
	18.54	0.802	16.7
	27.94	0.733	21.1
	38.10	0.601	16.3
	51.05	0.581	31.9
Commercial strand	12.7	1.037	14.6
Strand in polystyrene resin	6.60	2.281	7.3
	12.95	1.998	9.9
	18.54	1.507	16.1
	25.65	1.244	14.9
	37.85	0.788	20.4
	52.32	0.588	23.0
Commercial strand in polystyrene resin	12.7	1.604	8.4
Strand in epoxide resin ('Araldite AY 105')	6.10	3.180	2.7
	8.38	3.076	3.5
	11.18	2.807	7.7
	12.95	2.634	10.5
	16.76	2.516	6.2
	24.89	1.797	22.0
	37.08	1.307	22.7
	50.29	0.740	27.2
Commercial strand in epoxide resin	12.7	1.766	13.2
Strand in polyester resin ('Cellobond A 2622')	6.10	3.180	3.4
	10.92	3.069	3.8
	12.45	3.014	5.9
	18.54	2.710	7.6
	25.15	2.385	15.3
	36.83	1.977	23.0
	50.80	1.431	22.0
Commercial strand in polyester resin	12.7	1.749	14.9

For resin impregnated strand of constant glass cross-sectional area, the fibre diameter is of major importance. For the resins used there is an appreciable increase in the strand composite strengths as the fibre diameter is reduced.

The high strengths recorded for composites containing the thin fibres may be attributed to the fact that such fibres contain fewer external flaws and internal bubbles, and the total bonding area is much greater than that of a composite strand containing thick fibres. Further evidence of this is given by the fact that as the strengths increase, the scatter in the results falls appreciably.

For the resins used there is an increase in the strand composite strengths compared with those produced from commercial strand of a corresponding fibre diameter. This is probably due to the fact that the strand was embedded in the resin within minutes of production. In this series of tests no provision was made to protect the surface of the fibres by the application of a size or bonding agent, as is the usual practice in the production of commercial strand.
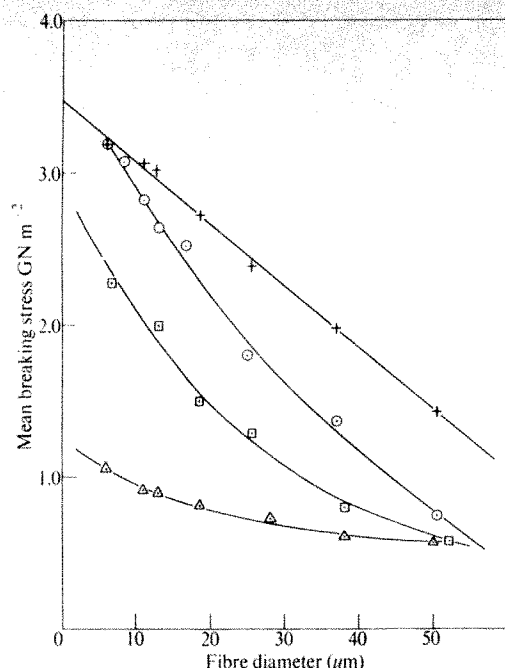
Fig. 1 Effect of fibre diameter on breaking stress in various resin matrices. △, Glass strand; ☐, strand in polystyrene; ○, strand in epoxide; +, strand in polyester.

The results indicate that if high strength composites are required, strand containing fibres of a diameter of about 0.005 mm should be used instead of the almost universally accepted fibre diameter of 0.013 mm. The final strength in the glass is in excess of 3.18 kN mm^{-2}, with little scatter. Extrapolation of the strength-diameter relationship for the polyester composite strand to infinitely fine fibres, as shown in Fig. 1, gives a mean breaking stress of just under 3.66 kN mm^{-2}, the strength of undamaged single fibres.

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Alternative Statement of the Second Law of Thermodynamics

As usually stated, the second law of thermodynamics is asymmetric under time reversal, and is thus not compatible with a microscopic mechanics symmetric under time reversal. In its most popular form, the second law states that the entropy of a closed system tends to increase. Attempts to derive this from time-symmetric physical laws are self-defeating because any argument which leads to increasing entropy may be time reversed to produce an equally valid argument leading to decreasing entropy. Yet irreversibility is a fact of life. This is Loschmidt's paradox[1].

The problem has lead to much discussion about the origin of the "arrow of time", some people believing that the laws of physics must be supplemented by an additional principle containing the seeds of irreversibility[2], others seeking some lack of temporal symmetry in the laws of physics themselves[3]; this problem has been discussed at length[4-7].

I agree with the view that our observations do not themselves imply any temporal asymmetry, so that there is no conflict with symmetric laws. This was known to Boltzmann[8] and has been discussed by other authors[6,7], yet it is not generally appreciated because we continue to state the second law in a form which is clearly asymmetric in time. Instead of shedding light on the traditional confusion among non-scientists regarding the apparent asymmetry of time, we have elevated it to the status of natural law. It is important to state the second law in such a way it is manifestly symmetric under time reversal. I propose that a proper generalization from our observations is: The entropy of a closed system tends to change monotonically with time.

A monotonic increase in entropy is certainly consistent with our observations, and so it is only necessary to establish that a monotonic decrease is also physically acceptable. If we were to observe a closed system whose entropy is decreasing monotonically it would not look like a film running backwards; we would not see familiar sequences of events in reverse order. This is because, by definition, to observe a closed system it is necessary to be within it. In fact the only closed system of which we have experience is that system of which the observable Universe is a part. We must ask how a monotonic decrease in entropy of a system appears to an observer who is a part of the system. Although familiar sequences of events may occur in reverse order, they will be observed in normal order by such an observer and will be physically acceptable to him, because an observer in such a system will "remember" the future rather than the past. The process of memory formation (or in general, of recording information), entails a net increase in the entropy of the system of which the observer (or recording machine) is a part. So in a closed system whose entropy changes monotonically, an observer remembers events which occur at times corresponding to lower entropy. The observations will be as acceptable in the case of monotonic decrease as in the case of monotonic increase. As an example of a system with monotonically decreasing entropy, imagine performing a complete time reversal on our Universe. This of course implies a reversal of our memory processes too, so that our observations would be utterly unchanged. Clearly, such a situation cannot be forbidden on thermodynamic grounds (though perhaps by weak interaction theory). If this simple point were to be made briefly in elementary text books on thermodynamics and statistical mechanics, much unnecessary heartache would be avoided.

It might be argued[9] that the statement which I propose is equivalent to the usual statement on grounds of logical consistency. According to this argument, if the entropy of a given closed system increases with time, then so must that of any other closed system. With such a parallelism of entropy increase one may define the future as the direction of time in which entropy increases. The parallelism is argued by constructing a composite isolated system consisting of several subsystems isolated from each other, and if some of the subsystems are increasing in entropy while others are decreasing, one will not in general maintain a monotonic change in entropy for the composite system. Such an eventuality is physically acceptable, however, because any observer in this system can observe events only in his own subsystem. Thus there are no observational grounds for demanding a monotonic change in entropy for such composite systems, and hence no evidence for the parallelism of entropy increase. Presumably in stating the law one should exclude composite systems by demanding a monotonic change of entropy for systems which are closed and multiply-connected only; that is those which cannot be divided into two or more parts permanently isolated from each other. Reichenbach's principle of the parallelism of entropy increase[6] refers not to systems which are permanently isolated from each other, but to hypothetical branch systems which are temporarily isolated from their surroundings. The increase in entropy of the branch systems during their period of isolation is a manifestation of the monotonic increase in entropy of the

Universe. It is precisely this parallelism in the behaviour of different parts of a system at different times that is at the heart of the second law.

How would one attempt to derive the second law, in the form proposed, from the laws of physics? One could imagine a simple generalization of the usual classical statistical argument in which one considers a system initially in a given macrostate and asks about the macrostate at some later time. If one counts all the phase space trajectories linking the initial macrostate to other macrostates, one is led to associate greater probability to those final macrostates with greater statistical weight. On the other hand, one could consider a system with a specified final macrostate, in which case a similar counting procedure implies that earlier macrostates must have greater statistical weight. This is hardly a satisfactory "proof" of the second law, and indeed there are those who would deny altogether the general validity of the second law, but would prefer to associate the monotonic increase in the entropy of our own system with non-thermodynamic features peculiar to it, such as cosmological expansion[4,7].

I thank Professor P. T. Landsberg, Dr P. J. Buttle and especially Professor R. B. Griffiths for helpful discussion.

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Consequences of Cycles in East African Climate

Western and Van Praet[1] have convincingly suggested that losses of yellow fever-trees in the Maasi Ambolesi are not due to over-population by cattle or elephants but to a climatic change causing a shift in the salt table. They assume that the change is part of a cycle, though of a much smaller range than has occurred in the past 10,000 yr. Perhaps inadvertently, they seem to suggest that the cycle producing the present vegetation change lasts about a century. Much shorter cycles than this may, however, be usual in the region, as evidence from further south suggests. It is important that this should be appreciated because, as the authors state, investment by governments on developments to accommodate tourists may be wasted if the climate is wrongly forecast.

Western and Van Praet cite evidence for synchronous changes in levels of lakes over a large area of East Africa, especially in those lakes that have no outlet to the sea; Rukwa is one of those lakes[2] and evidence from Lake Rukwa may be appropriate in the Maasi Ambolesi.

Rainfall or lake levels of Lake Rukwa, going back far enough, have not been recorded, so I have to rely on travellers' tales and inferences[3]. My information refers to rather few separate years but covers a century discontinuously. A dry period or a wet period, as indicated by lake levels, lasts several years. For example, Lake Rukwa has been very full from 1963 until

today, as it was for years around 1937. Between these two wet periods, the larger northern part of the lake has been so dry that in 1954 we could drive loaded 3-ton lorries across it. In earlier dry periods, when there were no mechanical vehicles to traverse the 30 miles of alkaline dust, the narrower parts of the lake bed could be crossed dry shod or ankle deep. In wet periods, 1,500 mile[2] or more of the northern lake was open to fishing from canoes. Table 1 shows reasonably well authenticated reports suggesting three or four cycles in a century.

Table 1 Available Information on State of Lake Rukwa, over 100 yr

Lake Rukwa	State	Author or authority[3]
1873	Dryish	Livingstone's last journey
1880–2	Very high	Joseph Thomson; Emil Kaiser
1892	Dry	Sir Harry Johnstone; Cross; Wallace
1904	High	Meyer
1920	Dry	Mateo
1933–42	High	Michelmore; Swynnerton; Bredo[4,5]
1954	Quite dry	Gunn[5]
1963–	Very high	Du Plessis; Kühne[5]

I found that upsurges of red locust populations in the Rukwa Valley have been associated with low levels of the lake[3]. Symmons[4] went further and showed a close relation between lake levels and cumulative deviation from average rainfall and a good correlation between locust numbers and previous rainfall; these have been used for forecasting locust numbers in Rukwa more than a year ahead[6]. It may have the salt-table mechanism proposed by Western and Van Praet and the cumulative deviation from average rainfall may also apply to both cases. If it does, sound planning for the Maasi Ambolesi may be facilitated.

On this very large scale, another consequence of climatic cycles is worth recording. During both recent periods of high level in Lake Rukwa, around 1937 and 1967, red locust breeding occurred on a threatening scale in Moçambique; such breeding has never been recorded there in years when Rukwa lake levels were low. Here, too, forecasting is worth attempting and perhaps also in other related matters in East Africa.

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BIOLOGICAL SCIENCES

Movement of Sodium Ions Associated with the Nerve Impulse

HODGKIN AND HUXLEY[1] calculated the extra sodium fluxes in the squid giant axon resulting from the passage of nerve impulses assuming that the time course of the observed currents represented the time course of a change in permeability. The net flux was in rough agreement with experimental data at room temperature but there was more exchange in the axon than in computed predictions. As the calculated fluxes increase by a factor of three when the temperature is reduced 10° it seemed appropriate to test the effect of temperature on the sodium fluxes.
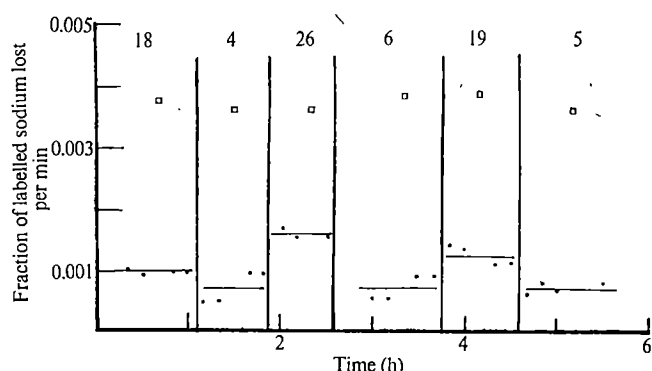
Fig. 1 The effect of temperature on the efflux of sodium from the resting (●) and stimulated (□) squid giant axon. The axon was loaded with radioactive sodium 2 h previous to this record by stimulating in radioactive seawater for 10 min at 150/s. During the stimulated collecting periods the axon was stimulated for the first 5 min of the 10 min period. Temperature is given in the numbers above each section of the experiment. 10 μM ouabain was present in the sea water throughout the experiment.

For influx experiments pairs of axons were dissected from *Loligo forbesi* and placed, uncleaned, in a chamber with 1–2 ml. of seawater made radioactive with ^{22}Na. The nerves were allowed to soak for 5–10 min and then one nerve was stimulated 50 times per second for 10–30 min. The nerve impulses were continuously monitored with external electrodes and an oscilloscope. A sample of the radioactive seawater was taken, the excitability of the control nerve checked, and then the ends of the axons were cleaned and the axoplasm extruded[2], weighed and counted in a well scintillation gamma counter. The difference between the two axons was taken as the extra influx due to activity. The experiments were performed either at room temperature (20–22° C) or in a constant temperature room (6–7° C). The results are given in Table 1. The observed extra influx at low temperature is actually smaller than at high temperature instead of much larger as predicted by Hodgkin and Huxley. The extra influx found at room temperature is similar to other observations in squid axons[3].

Table 1 Extra Influx of Sodium Associated with Nerve Impulses Expressed in pmol cm^{-2}-Impulse ± Standard Error.

	6–7° C	20–22° C	Q_{10}
Observed values	3.4±0.8 (5)	5.9±1.1 (6)	1.5
Predicted value for membrane action potentials. Hodgkin and Huxley[1] Table 5	19.3	5.0*	1/3

* Computed for 18.5° C.
Number of experiments in parentheses.

In a few preliminary experiments the efflux of sodium ions was measured by a method similar to that of Hodgkin and Keynes[8]. The axon was cleaned, loaded by stimulating in radioactive seawater and placed in a water-jacketed tube. The amount of tracer leaving the nerve per unit time was measured by collecting seawater which flowed continuously over the nerve. A typical experiment is shown in Fig. 1 where the fraction of the radioactive isotope leaving the axon per minute is plotted against time. One can easily see that the rate of efflux does not increase threefold for a 10° C reduction of the temperature.

Although there are no published experiments directly measuring the stimulated fluxes as a function of temperature, there is indirect evidence which supports the present findings. In an experiment at 7.5° C, using an indirect method, Moore and Adelman[4] found only 1.5 pmol cm^{-2}-impulse for the net influx whereas the theory of Hodgkin and Huxley predicts several times this much. In the data given in Table 5 of Hodgkin and Huxley no change had been seen in the net

influx of sodium over a range of 8° C although a Q_{10} of 1/3 predicts that more than twice as much sodium should enter at the lower temperature. In the rabbit vagus nerve there is evidence that the total amount of sodium gained by the fibre per impulse is largely independent of temperature[5].

These data seem to rule out any model of the nerve membrane which accounts for the current by a simple change in permeability. At low temperatures the nerve impulse has a much longer duration, the time course of the voltage clamp currents are greatly prolonged, and so the predicted ionic fluxes are considerably larger. This is true whether the permeability change is brought about by an alignment of particles[1] or the opening of a pore[6]. This suggests that a new way of thinking about the observed currents is necessary.

I have recently proposed an explanation of the ionic currents based on a consideration of space charge limitation[7]. In this model the amount of sodium which moves during the nerve impulse is limited to the amount in the membrane before the impulse. The passage of an impulse leaves the membrane depleted of sodium which makes the nerve refractory. As a first approximation one would not expect the content of the membrane phase to vary dramatically with temperature. It was this consideration which led to these flux measurements.

My explanation predicts that the membrane sodium content, and thus the extra sodium influx, should increase with increasing temperature. The ions enter the lipid phase rather as electrons enter the vacuum of a thermionic diode. At higher temperatures more ions will be able to overcome the interface potential energy barrier (analogous to the work function in a metal) and enter the lipid phase of the membrane. From the data presented here one can calculate a potential barrier of 0.28 eV corresponding to the observed Q_{10} of 1.5. It is interesting to note that in *Sepia* axons the resting sodium influx increases with a temperature coefficient of about this size[8] as does the maximum sodium conductance ($\bar{g}_{Na}$) in the squid axon[9] as one might predict because they also should vary with the number of current carriers in the membrane phase.

How, then, are the prolonged voltage clamp currents at low temperatures explained in terms of the space charge limited model? As indicated previously[7] the kinetics of a space charge limited diode are temperature dependent because at higher temperature the ions have more thermal kinetic energy and enter the membrane with a higher average initial velocity. Because the ions enter with a non-zero initial velocity they tend to accumulate inside the membrane and form a potential maximum. (In discussions of vacuum diodes this is a potential minimum because electrons with a negative charge carry the current instead of positively charged ions) and is referred to as a "virtual cathode"[10].

The virtual cathode behaves as a source of charge carriers. At high temperatures the ions enter with a higher initial velocity, the potential maximum is closer to the far side of the membrane and thus the distance travelled by the ions during the voltage clamp pulse is shorter. This means that the transit time is less and the currents change more rapidly. At low temperatures the ions travel further in the membrane. As shown in Fig. 2, the same number of ions can produce current for a longer time by travelling a longer distance. Thus the flux, as measured by radioactive tracers, is not equal to the time integral of the current observed in the external circuit. This is different from the situation found in metals or electrolyte solutions because in both cases the spatial distribution of charge carriers is uniform and does not vary with time. The difficulties in applying Kirchoff's rules to this system also arise from this difference in charge distribution. At first it may seem somewhat surprising to suggest that a relatively large amount of free charge is in the lipid phase. However, it has been quite convincingly shown that substances commonly considered insulators can carry large currents if they have been provided with suitable,
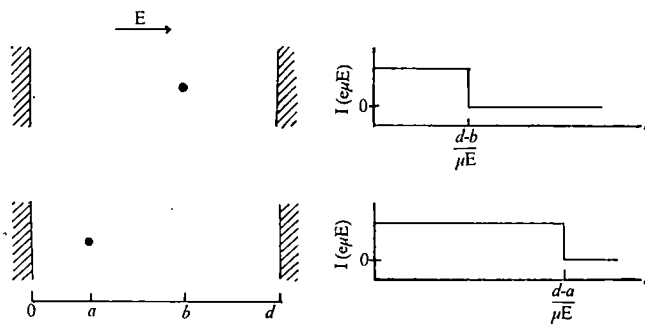
Fig. 2 The current associated with a single positive ion moving through a dense medium. The electric field is applied at $t=0$ with the ions (●) starting at the positions indicated. The current, I, measured in the external circuit for one ion is the charge on the ion, e, times its drift velocity (the mobility, μ, times the field strength, E). The current persists as long as the ion is between the electrodes, that is, between the two aqueous phases. The transit time is the distance travelled divided by the drift velocity.

low work function, electrodes[11],[12] The work function of a metal can be altered by dipoles or charges at its interface. Presumably this also occurs at the cell's aqueous-lipid interface.

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Currents Related to Movement of the Gating Particles of the Sodium Channels

"... IT seems difficult to escape the conclusion that the changes in ionic permeability depend on the movement of some component of the membrane which behaves as though it had a large charge or dipole moment"[1]. With these words Hodgkin and Huxley predicted the existence of gating currents: charge movement associated with molecular rearrangements that attend the opening and closing of the ionic channels in response to changes in the membrane field. The polarity of gating current of the sodium channels can be easily predicted: following a positive step change of membrane voltage, positively charged gating particles would move outward through the membrane field from closed to open position (or negatively charged particles would move inward), yielding an outward current. On repolarization after a voltage step that opened the channels, gating current would be inward, as particles moved from open to closed position. Hodgkin and Huxley were unable to
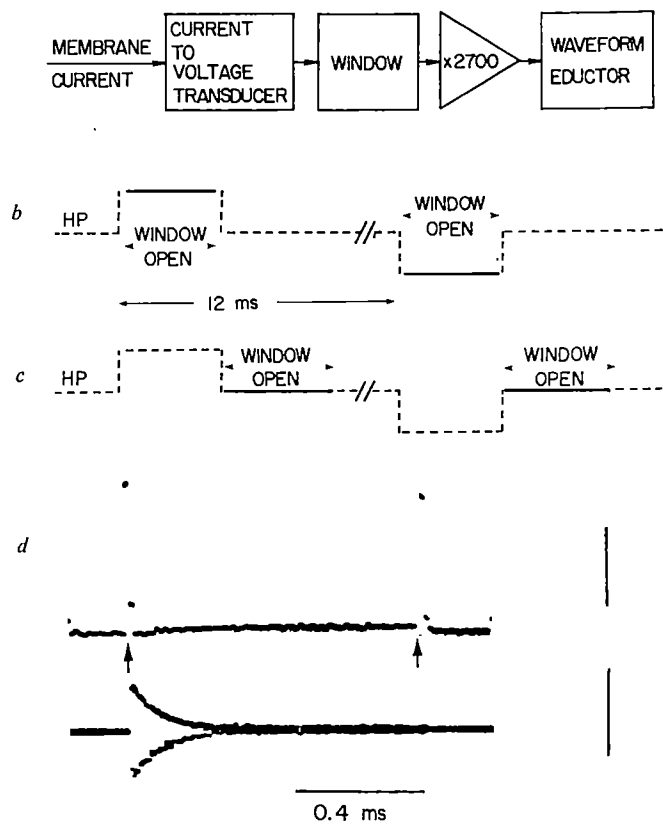
Fig. 1 *a, b, c,* See text. *d,* Lower trace: current resulting from a positive and a negative voltage pulse applied to a passive RC circuit. The calibration bar is equivalent to 2.5 pA μm^{-2}. Upper trace: averaged and summed current for 4,000 positive and 4,000 negative pulses. The calibration bar is equivalent to 0.05 pA μm^{-2}. The window opened 30 μs after the beginning of the pulse (left arrow) and closed at the right arrow.

observe gating currents experimentally, and concluded that the density of ionic channels in the membrane must be low. A later attempt by Chandler and Meves[2] to detect such currents was also unsuccessful, and they estimated that there are less than 100 sodium channels μm^{-2}, a prediction that has been borne out by later estimates of sodium channel density[3],[4]. We report here that by use of signal averaging techniques, we have observed small transient currents which we believe are the gating currents of the sodium channels.

Our experiments were performed on isolated squid giant axons, which were internally perfused and voltage clamped. A major technical problem is that the expected gating currents should be obscured by the relatively enormous capacitative and ionic currents. To minimize ionic currents we perfused the interiors of the fibres with a solution containing Cs^+ ion, which is impermeant, in place of K^+ ion, and we replaced external sodium with the impermeant ion Tris. In many experiments the external medium also contained 2×10^{-7} M tetrodotoxin to suppress ionic movement through sodium channels. There remains nonetheless a substantial ionic current (leakage) on which the gating currents are superimposed. The leakage current was large enough to saturate our amplifiers, but fortunately it is time invariant, and we eliminated it by feeding an offsetting current into the current to voltage transducer (see below).

Imperfections in the membrane dielectric of the squid giant axon (a small portion of which may arise from gating particle movement) cause a slow tail of capacitative current which is large compared with the anticipated gating currents. Most of this tail current was eliminated by algebraically summing the current from exactly matched pulses of opposite sign. The remaining current is not symmetrical for pulses of opposite sign, and may be gating current. In practice positive and
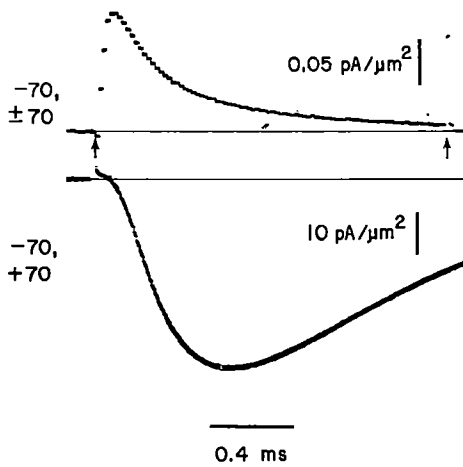
Fig. 2 Sodium current (lower trace) and presumed gating current (upper trace: procedure of Fig. 1b) from the same axon. For the lower trace the axon was in artificial seawater and internally perfused with 275 mM KF+400 mM sucrose, at 3.5° C. Upper trace: averaged current for pulses of ±70 mV from a holding potential of −70 mV. The axon was in Tris seawater, internally perfused with 550 mM CsF, at 3.5° C. The window opened 20 μs after the beginning of the pulse (left arrow) and closed at the arrow on the right. Tris seawater was K-free.

negative pulses were alternated at 12 ms intervals, as shown in Fig. 1b and c. To prevent saturation of our amplifiers by the very large signal representing the early part of the capacitative current transient, we devised a "window" (Fig. 1a) which shut out the first 10–30 μs of the signal following a voltage step, as illustrated in Fig. 1b and c. The signal passing through the window was amplified and fed to a Princeton Applied Research Waveform Eductor, which performed the dual function of algebraically summing the currents and averaging them. Each of our records is the average of current from several thousand pulses of each polarity. The apparatus was tested by applying alternating pulses to a passive RC circuit designed to give tail currents of about the same amplitude and time course as those recorded from the membrane. The results of a test are shown in Fig. 1d. The lower traces show the current for a positive and a negative pulse, with the first 30 μs after the beginning of pulses excluded by the window. The upper trace shows the averaged sum of current for 4,000 positive and 4,000 negative pulses. The first point after the opening of the window (representing 10 μs) is seriously misplaced and the next bit is slightly so, but after these the current sum is zero. Thus nothing resembling gating currents are observed when pulses are applied to a circuit composed of ordinary capacitors, which shows that the apparatus functions well and introduces minimal artefact.

The upper trace in Fig. 2 shows what we think is predominantly gating current of the sodium channels. The trace is the algebraically summed, average current for 2,000 positive and 2,000 negative pulses of 70 mV amplitude, from a holding potential of −70 mV. The window opened at the arrow on the right, 20 μs after the beginning of the pulse, and remained open until just before the beginning of the step back to the holding potential (procedure of Fig. 1b). Each point on the trace gives the average current during a 20 μs interval. The current rises for 80 μs (four points) to a peak amplitude of 0.13 pA μm^{-2} and then declines toward a steady level set by the leakage current. This level is approximated in the figure by the thin line. The transient is outward in direction, and its time course is rapid in comparison to the sodium current (lower trace, Fig. 2) recorded from the same axon in conventional solutions (artificial seawater outside, KF inside). The maximum amplitude of the sodium current is about 300 times that of the presumed gating current.

The average current shown in Fig. 2 is almost certainly the sum of inward current during the negative pulses and outward current during the positive pulses. We think that the rising

phase is due to the rapid decay of a negative (inward) current, and that the outward component, seen alone, would rise instantaneously and decay monotonically. In theory if the holding potential were more positive, more of the gating particles would be in the open position at the holding potential, and the inward current during the negative pulses would be larger than for a more negative holding potential. Fig. 3a, b, and c shows the results of an experiment to test this point. Summed and averaged current is illustrated for three holding potentials, and the thin lines give the current level approached by the end of the trace. For a holding potential of −50 mV there is a conspicuous transient current that is inward relative to the steady level, followed by a small outward current; while at −70 mV there is almost no inward current and a larger outward current, just as expected. At a holding potential of −100 mV (Fig. 3c) the rising phase is almost absent, again as expected, for in this case almost all of the gating particles are in closed position at the holding potential.

In the procedure just described, the dominant charge movement for steps from a holding potential of −70 mV occurs during the positive pulse and is outward. At the end of the positive pulse there should in theory be inward charge movement, as gating particles move back from open to closed
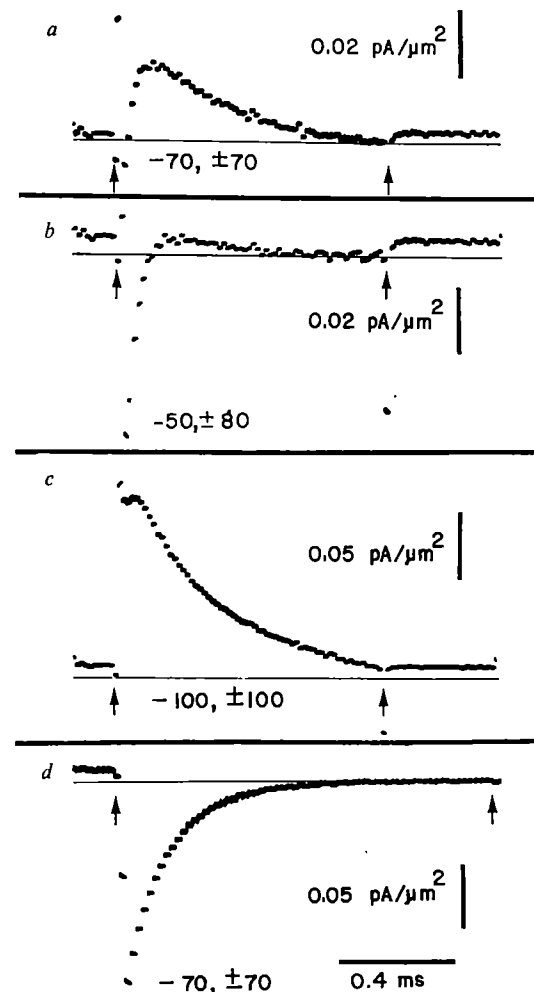
Fig. 3 a, b, c, Presumed gating currents during pulses of the indicated amplitudes (±y), from the indicated holding potentials (−x) (procedure of Fig. 1b). The window opened 20 μs after the beginning of the pulses. Tris seawater+2×10^{-7} M tetrodotoxin, internally perfused with 550 mM CsF, at 2° C. d, Gating currents at the end of pulses of 70 mV amplitude from a holding potential of −70 mV (procedure of Fig. 1c). The window opened 20 μs after the end of the pulses. Tris seawater+ 2×10^{-7} M tetrodotoxin, internally perfused with 275 mM CsF + 138 mM KF+200 mM sucrose, at 2° C. a, b, c, from one axon, d, from another. Arrows indicate opening and closing of the window. Tris seawater was K-free.

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position. Charge movement during the negative pulse is relatively small, and the outward current expected at the end of the negative pulse should be overshadowed by the relatively large inward movement at the end of the positive pulse. When the window is opened after the pulses (procedure of Fig. 1c) an inward current is in fact observed (Fig. 3d), primarily reflecting, we think, the closing of gates after the positive pulse.

In theory the sum of gating charge movement during steps of, for example, ± 70 mV should be equal but opposite in sign to the sum of movement after the steps, as particles displaced by the pulses return to positions appropriate to the holding potential. In two experiments to test this, the movement during the pulses differed from that after by only 2% in one experiment and 8% in the other. This provides strong evidence that the observed currents are due to charge movement within the membrane, for it is highly improbable that ionic movement through the membrane channels during the pulses would exactly equal in magnitude ionic movement after them. Additional strong evidence that the observed currents are not ionic movements through the sodium channels is the fact that they are unaffected by tetrodotoxin.

The evidence that it is gating charge movement is as follows. (i) Experiments on axons not poisoned with tetrodotoxin show that the current patterns illustrated above are obtained only from axons that have a normally functioning sodium permeability, both before and after the averaging procedure. Some axons give a different pattern, an inward current in all circumstances, but this pattern is always correlated with a high leakage current and with the absence of normal sodium permeability on return to artificial sea water outside and KF inside. (ii) The charge movement has a rapid time course that is compatible with changes leading to the opening of the activation gates of the sodium channels. The time course of the charge movement is too rapid for it to be readily associated with inactivation of the sodium permeability or activation of the potassium permeability, which are relatively slow processes. Also, because they are slow, gating current associated with these processes would be relatively small (unless the total charge movement is unexpectedly large) and their contribution to the observed current is thus probably minor. The absence of a tetrodotoxin effect on presumed sodium channel gating currents may seem surprising, but is not unexpected, for tetrodotoxin has no effect on g_{Na} kinetics[5,6]. Our evidence seems to confirm that tetrodotoxin blocks the sodium channels without altering the operation of their gates. (iii) The dependence of the amplitude and shape of these currents on holding potential and pulse size agrees qualitatively with the behaviour expected of particles responsible for the activation of the sodium permeability. (iv) The net charge movement is consistent with estimates of Na channel density. From the dependence of sodium permeability on voltage it has been estimated that the gating particles that activate each Na channel have a net charge equivalent to that of six electrons[1]. For a holding potential of -100 mV and pulses of ± 100 mV, the net charge movement in our experiments is about 300 electronic charges/μm^2. Dividing this figure by six electronic charges/channel, one obtains 50 channels/μm^2, in reasonable agreement with estimates derived from studies of tetrodotoxin binding to other axonal membrane[3,4].

Recently, Schneider and Chandler[7] have successfully recorded intramembrane charge movement in muscle fibres which may be related to excitation–contraction coupling. The charge movement they observed is somewhat larger and slower by almost two orders of magnitude than that reported here, altogether too slow to be related to gating of the action potential permeabilities.

Our results support the hypothesis that permeability changes are brought about by the movement of charged particles or dipoles within the membrane in response to changes in the membrane potential.

We thank Dr E. Rojas for first interesting us in attempting to measure gating currents, and for his collaboration in early

attempts to do so, and Dr Clara Franzini-Armstrong for dissecting many of the axons.

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Contractile Effects of a Calcium Ionophore

THE contractile state of muscle is controlled through variations of the intracellular concentration of calcium ion[1-3]. In different types of muscle, Ca^{2+} transients inside the fibres are sustained to various degrees by calcium movements to and from intracellular stores, such as the sarcoplasmic reticulum (SR). In skeletal muscle, the activity of SR is sufficient to account for release and uptake of intracellular calcium, fulfilling concentration and time requirements for a single twitch. But it is not as well developed in cardiac and even less so in smooth muscle.

The role of calcium in excitation–contraction coupling has been explained and verified with a variety of physiological and biochemical techniques, involving simple contractile systems, subcellular fractions, and purified proteins. No satisfactory method for a specific interference with this control system in whole muscle, however, has yet been discovered. Caffeine[4] and Ryanodine[5], two agents whose contractile effects have been attributed to alteration of calcium transients, are only partially effective on isolated SR, and their molecular mechanism of action is still unknown.

We have found that the calcium ionophore X-537A, at μM concentrations, causes rapid release of accumulated calcium from SR vesicles[6,7] and has marked contractile effects in isolated preparations of skeletal, cardiac and vascular smooth muscle. X-537A is an antibiotic obtained from an unidentified streptomycete[8] whose structure[9] is given in Fig. 1. The antibiotic is known to bind divalent cations; its barium complex was studied by X-ray diffraction[10], and shown to be made of two antibiotic molecules encircling one barium ion and one water molecule, stabilized by coordination and hydrogen bonding. The complex has a spherical shape, enclosing the ion in a hydrophilic pocket, while the exterior is non-polar and lipophilic, and for this reason, X-537A increases the
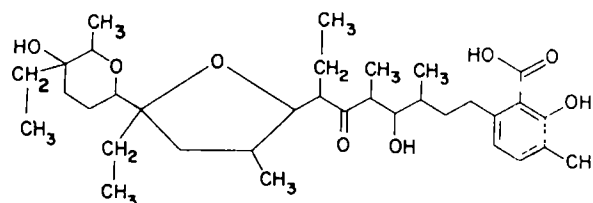
Fig. 1   Structure of X-537A.

Fig. 2 *a*, Calcium accumulation by SR vesicles, followed by X-537A induced release. *b*, Steady state levels of calcium accumulation by skeletal (●) and cardiac (○) SR, in the presence of different concentrations of X-537A. SR was prepared and calcium accumulation was measured at 25° C in the presence of 20 mM histidine, *p*H 7.0, 80 mM KCl, 5 μM MgCl₂, 5 × 10⁻⁵ M ⁴⁵Ca-CaCl₂ and 350–400 μg SR protein ml.⁻¹. The reaction was started by the addition of 2.5 mM ATP, and stopped by 'Millipore' filtration[12].
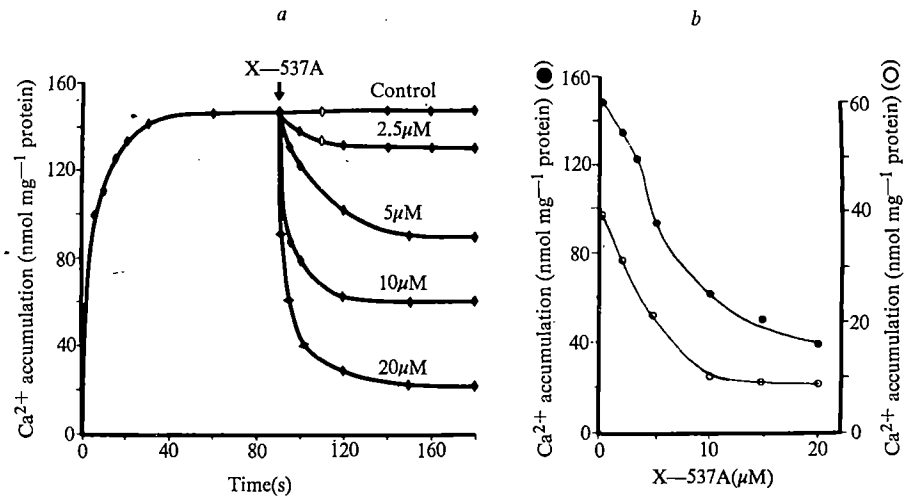
permeability of artificial and natural membranes to divalent cations[11].

Addition of the ionophore to SR vesicles previously filled with calcium through the action of the membrane pump results in rapid release of the accumulated calcium. An identical concentration dependence of this effect is obtained in both skeletal and cardiac SR (Fig. 2). These concentrations produce increased resting tension and contracture in both twitching and quiescent diaphragm strips (Fig. 3). The effect is maximal in approximately 10 min and therefore its onset is slower than observed in isolated SR vesicles, probably due to slow penetration of the ionophore into the muscle fibres.
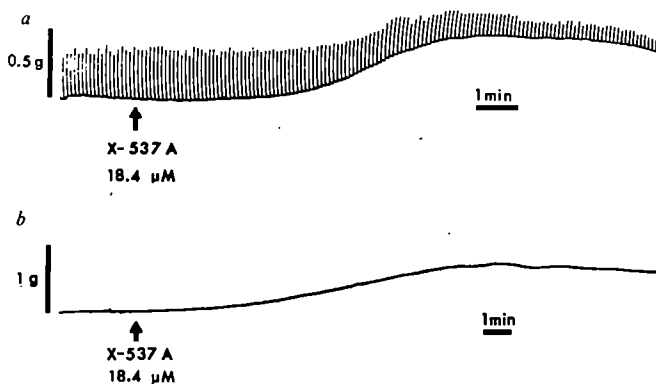
Fig. 3 Isometric tension of isolated strips of rat diaphragm. Bathing solution, 118 mM Na Cl, 4.75 mM KCl, 2.54 mM CaCl₂, 1.19 mM MgSO₄, 1.19 mM KH₂PO₄, 12.5 mM NaHCO₃, 5.56 mM glucose. Gassing mixture 95% O₂–5% CO₂ at 37° C. Muscle length was adjusted to obtain maximal tension development. *a*, Muscle stimulated directly with a suprathreshold current, of 3 ms pulse duration; *b*, muscle was not stimulated.

Time resolution of single contractile cycles (Fig. 4) shows that while the resting tension is increased and the twitch tension decreased by the ionophore, the times of peak tension development and decay are unchanged.

Considering present knowledge on the regulatory role of calcium on the contractile state of myofibrils, one expects that a calcium ionophore, entering a muscle fibre, would induce a state of contracture by altering intracellular calcium gradients and interfering with physiological modulations of calcium concentrations. This in fact was observed in skeletal muscle preparations.

The ionophore was effective both in twitching and quiescent muscles, so the observed contractile effect was therefore not dependent on an alteration of the membrane action potential.

Because X-537A is active in SR vesicles and on whole muscle preparations within the same range of concentrations, we might speculate that the calcium sequestering ability of SR

is also impaired by the ionophore in whole muscles, and is directly involved in the development of contracture induced by the ionophore. On the other hand, this effect may also be produced by an increased permeability to calcium in the surface membranes of the muscle fibres.

Our experiments indicate that resting and twitch tensions, but not the times for peak tension development and decay, may be altered by interfering with transmembrane calcium gradients and by raising the steady state concentrations of intracellular calcium ion.

Contrary to experiments with skeletal muscle, those with cardiac preparations yielded more complex results. On electrically driven rabbit heart left atria and guinea-pig ventricular strips, low concentrations of X-537A (2.5 – 5.0 μM) produced a positive inotropic effect (Fig. 5), characterized by
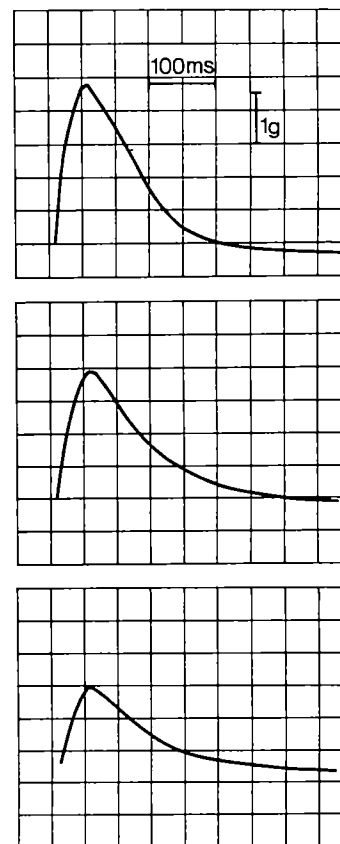
Fig. 4 Oscilloscopic traces of single twitches of rat diaphragm strips. Experimental conditions as in Fig. 3, except bath temperature was 25° C. From top to bottom: before, 3 and 6 min after addition of X-537A (20 μM).
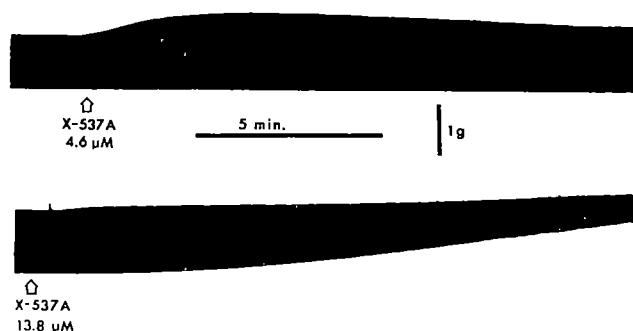
Fig. 5 Isometric tension of isolated rabbit atrium[13]. Bath solution as in Fig. 3. The muscle was stimulated with square wave stimuli of 5 ms duration, at 3 times threshold current, at a frequency of 2.0 Hz.

increased twitch tension, and no change either in times of peak tension development and decay or in resting tension. The inotropic effect was transient and could not be repeated by further additions of ionophore. After its occurrence, the cardiac preparations were not responsive to catecholamine releasing agents such as tyramine, but were still responsive to isoproterenol and norepinephrine. The positive inotropic effect of X-537A was not obtained after beta-adrenergic blockade with propranolol, or depletion of catecholamines by pretreatment of the animals with reserpine.

All of this evidence indicates that, in cardiac muscle, the positive inotropic effect at low concentrations (2.5–5.0 μM) of X-537A is due to release of endogenous catecholamines. The release may be related to the ability of X-537A to complex and transfer catecholamines across organic phases[11].

On the other hand, in cardiac preparations (Fig. 5), the ionophore at concentrations (5–20 μM) equal to those effective in skeletal muscle and in SR vesicles, produces increased rest tension and contracture. This is best observed in the presence of beta-adrenergic blockade, when the transient inotropic effect is absent and the effect of the ionophore is analogous to that observed in skeletal muscle. In this way, the catecholamines and calcium mediated effects can be differentiated.

As reported by Pressman[11], in smooth muscle (rabbit aortic strips), X-537A produces a transient contraction followed by a slight elevation of resting tone. We found that in the absence of endogenous catecholamines (that is reserpinization) the transient contractile tension response to the ionophore was attenuated, but elevation of resting tension persisted.

The calcium ionophore properties of X-537A are reflected in its contractile effects on isolated muscle preparations. The ionophore, at concentrations inducing total release of accumulated calcium from SR vesicles, produces contracture or increased resting tension in skeletal (3–6 g tension/100 mg wet weight), cardiac (2–3 g tension/100 mg wet weight) and smooth (0.4–0.6 g tension/100 mg wet weight) muscles.

In addition, very low concentrations (2.5 μM) of X-536A induce a positive inotropic effect in cardiac preparations and the occurrence of contraction in smooth muscle. These transient effects are mediated by release of endogenous catecholamines, and are not obtained in skeletal muscle.

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Active Transport of L-Dopa in the Intestine

In a discussion of the problems associated with the metabolism and absorption of L-3,4-dihydroxyphenylalanine (L-dopa) in patients with Parkinson's disease[1], Bianchine et al. suggested that the small intestine is the major site of absorption, as is the case with many other amino-acids. The existence of a carrier-mediated transport process was implied by the suggestion that the absorption of L-dopa is subject to competitive inhibition by other amino-acids. But a study[2] of the absorption of ${}^{14}C$-L-dopa *in vitro* by sacs of everted rat intestine did not suggest an active transport mechanism. On the contrary, there was no significant difference in mucosal uptake when the tissue was gassed with oxygen or rendered anoxic with nitrogen. These data appeared to be consistent with a passive diffusion mechanism for the entry of L-dopa into the mucosa of both stomach and small intestine. On the other hand, there is evidence that L-dopa inhibits the absorption of L-phenylalanine and L-tyrosine in patients with Parkinson's disease[3]. We have now investigated whether there is an active component in the L-dopa transport mechanism in the small intestine of the rat *in vitro*.

Male Sprague-Dawley rats (250–300 g) fed *ad lib.* were killed by a blow on the head. The small intestine between the common bile duct and the caecum was removed quickly, washed through with 20 ml. of normal saline and everted on a length of polythene tubing. Within 5 min of the death of the animal, the everted intestine was incubated at 37° C in Krebs-Ringer bicarbonate buffer in the oxygenated organ bath system of Wade and Bauckham (manuscript in preparation). The technique is a modification of that described by Fisher and Parsons[4], but differs in that the whole of the small intestine is used and is everted before incubation. The mucosal fluid is continually oxygenated while a constant circulation of serosal fluid is maintained. The system also facilitates sampling from either side of the intestine at any time.

Initial serosal and mucosal volumes were 40 ml. and 60 ml. respectively, and the duration of each experiment was either 30 or 60 min. Tissues were oxygenated by gassing continuously with oxygen (95%) and carbon dioxide (5%) and rendered anoxic by replacing the gas mixture with nitrogen. All incubation media contained D-glucose (250 mg%).

L-Dopa was assayed by gas liquid chromatography. Aliquots of acidified incubation media (0.2 ml.) were evaporated to dryness on a rotary evaporator at 40° C. The trifluoroacetate derivative was prepared by dissolving the residual L-dopa in 0.2 ml. of tetrahydrofuran and adding
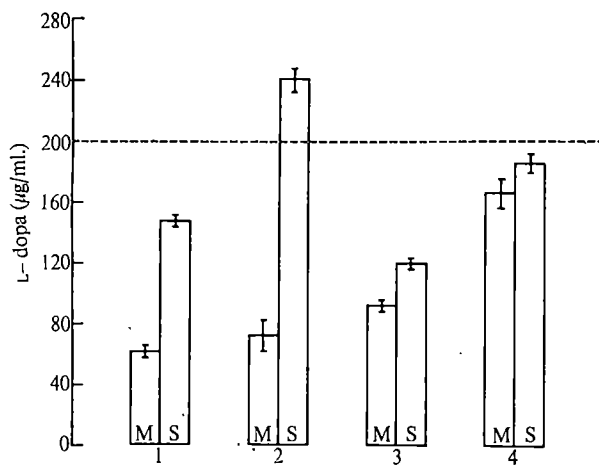
Fig. 1 The effects of anoxia and Ro4-4602 on the concentration gradients of L-dopa established after 60 min of incubation. At least four animals were in each group and the column heights indicate the mean values ± the standard error of the mean. M, Concentration in mucosal fluid; S, concentration in serosal fluid. Groups 1 and 2 gassed with 95% O_2, 5% CO_2; groups 3 and 4 gassed with nitrogen; groups 2 and 4 contained 200 µg/ml. Ro4-4602 in both mucosal and serosal media. The initial concentration of L-dopa in both mucosal and serosal media is shown by the dotted line.

When the experimental period was reduced from 1 h to 30 min and L-dopa was omitted from the serosal side, there was no inhibition of mucosal uptake in the presence of Ro4-4602 alone (Table 1), while the additive inhibitory effect of anoxia remained highly significant.

Table 1 Mucosal Uptake of L-Dopa *in vitro*

Isomer	Alteration to standard incubation conditions	No. of expts.	Conc. of L-Dopa in mucosal fluid at 30 min (mean±s.e.) µg/ml.
L-Dopa	—	5	90±6
	Ro4-4602	5	94±5
	Anoxia	4	141±7
	Anoxia + Ro4-4602	3	166±6
	15 mM L-leucine	3	177±6
	10 mM D,L-phenylalanine	2	126±2
D-Dopa	—	4	171±2

All incubations were carried out in Krebs-Ringer bicarbonate buffer, *p*H 7.4 at 37° C, containing glucose (250 mg%). Incubation media were gassed with oxygen (95%) and carbon dioxide (5%) or rendered anoxic with nitrogen. Leucine and phenylalanine were present in the mucosal fluid only. Ro4-4602 was present on both sides of the intestine. Initial concentration of L-dopa in all experiments was 10^{-3} M.

0.03 ml. of trifluoroacetic anhydride. After at least 10 min at room temperature, 5 µl. aliquots of the reaction mixture were injected into a Bendix series 2500 gas chromatograph fitted with a flame ionization detector. Chromatography conditions were as follows. The column was of glass 6 feet long, with an inner diameter of 4 mm; it was packed with 6% QFI (trifluoropropyl methylsilicone polymer, Supelco Inc., Bellefonte, Pennsylvania) on Supelcoport 100/120 mesh. The temperature of the column was 155° C, of the inlet 165° C, and of the detector 165° C. Nitrogen carrier flowed at a rate of 50 ml./min, hydrogen at 40 ml./min and air at 200 ml./min. Relevant standards were included in each series of assays.

Beginning with 200 µg/ml. (10^{-3} M) L-dopa on both sides of the intestine, a concentration gradient was evident after 60 min of incubation (Fig. 1). The capacity of the small intestine to degrade L-dopa has previously been demonstrated in the rat[2]. The extent of intestinal degradation of L-dopa in the present experiment was reflected by the fall in concentration of the drug on both sides of the intestine. The decrease in concentration on the serosal side was significantly inhibited by the addition of an L-dopa decarboxylase inhibitor (N-(DL-seryl-N¹-2,3,4-trihydroxybenzyl)-hydrazine (Ro4-4602, 20 mg%, Hoffmann-La Roche) to the incubation media at the beginning of the experiment.

In the presence of the decarboxylase inhibitor, the concentration of L-dopa in the serosal fluid increased beyond the starting concentration while the mucosal uptake was not significantly influenced. Anoxia markedly reduced the gradient developed, indicating some dependence on oxidative metabolism (Fig. 1).

The separate and combined effects of anoxia and Ro4-4602 provide further insight into the mechanism of mucosal uptake of L-dopa. When the supply of oxygen was maintained, inhibition of the enzymatic decarboxylation of L-dopa had only a slight effect on mucosal uptake after 1 h. In the anoxic preparation, however, inhibition of L-dopa metabolism markedly inhibited mucosal uptake. This suggests that enzymatic decarboxylation has a regulating effect on the passive diffusion of the drug into the intestinal mucosa by its influence on the concentration gradient. On the other hand, "active" uptake seems to be the rate-limiting factor in the movement of drug into the oxygenated gut, with passive diffusion playing only a minor role.

Other data (Table 1) show that the uptake of L-dopa has two further characteristics of an active transport process. Inhibition of uptake by other amino-acids was demonstrated by the marked decrease in the rate of disappearance of L-dopa from the mucosal fluid when in the presence of 15 mM L-leucine. The inhibition was significant but less marked in the presence of 10 mM D,L-phenylalanine. Second, comparison of the absorption rates of D-dopa and L-dopa showed that the latter was more readily absorbed. This was in accord with data[5] which clearly demonstrated the stereospecificity of intestinal amino-acid transport, such that only the L-isomers of most of the naturally occurring amino-acids were absorbed by an "active", saturable mechanism.

Preliminary experiments in this laboratory on the kinetics of mucosal uptake of L-dopa indicate that the relationship between the reciprocals of initial rate of uptake and initial concentration is characteristic of a saturable process of the Michaelis-Menten type (Fig. 2). Extrapolation for the trans-
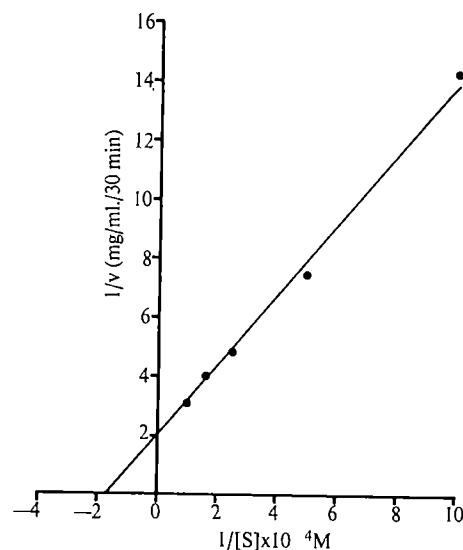
Fig. 2 The uptake of L-dopa by the everted small intestine of the rat shown as a Lineweaver-Burk plot. The half-saturation constant (K_t) is 5.9 mM.

port constant (K_t) gave a half-saturation concentration of 5.9 mM.

We interpret the data discussed here as evidence for the existence of an active transport mechanism for the intestinal absorption of L-dopa. The drug can be accumulated against a concentration gradient. Its absorption can be inhibited by anoxia and the presence of other amino-acids. The L-isomer is absorbed preferentially and its absorption appears to be saturable and characteristic of a carrier mediated or other saturable process.

The existence of a similar L-dopa absorptive mechanism in man may explain some of the problems associated with the absorption and the bioavailability of various dose forms. A relatively slow absorption rate from the stomach, where active transport of nutrients has not been demonstrated, would be predicted. Further, it would be expected that protein and perhaps other foodstuffs taken with an oral dose of L-dopa would inhibit the absorption of the drug from the intestinal lumen. Such an effect has been demonstrated on the absorption of tryptophan in man[6]. Being one of the few drugs absorbed by active transport, L-dopa would be subject to a greater variety of bioavailability effects than drugs which are absorbed by passive diffusion alone.

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Event Related Slow Potential Changes in Human Brain Stem

A SLOW negative shift of brain electrical potential can indicate association made between paired stimuli when one acts as a warning and the other an imperative stimulus[1]. This is termed the contingent negative variation (CNV). Intracerebral recording in man confirmed the cortical origins of the change seen at the scalp. There have, however, been suggestions based on animal studies[2-5] that, although essentially a cortical change, the CNV might be mediated by the action of sub-cortical centres, possibly in the thalamus and/or the brain stem and midbrain reticular system. Haider et al. recording from electrodes in thalamus and on the cortex of patients undergoing acute thalamic surgery, have reported characteristic changes in evoked potentials from the ventro-oral nucleus accompanying the appearance of the CNV at the cortex[6,7].

Recently the opportunity arose for us to study such responses in two patients with electrodes implanted in brainstem structures. Although electrode placement was not identical in both cases the overall distribution of electrodes was very similar. For convenience the results presented have been drawn from one patient, the general pattern of findings being almost identical in the two cases.

The patient was a 57 yr old woman who had suffered a cerebral thrombosis two years previously giving rise to a moderate left hemiparesis and the appearance of a thalamic syndrome. There was painful hyperaesthesia with sensory impairment over the entire left half of the body and face. Thirty-four 150 μm diameter gold electrodes had been implanted in the brain using stereotaxic procedures in preparation for treatment for the condition of intractable pain. The electrodes were in five sheaves which straddled the right thalamus. Each electrode was 4 mm long and separated from the next by 2 mm. Locations were estimated on the basis of X-ray photographs and the calculation of distances from known reference points[8]. On this basis the most rostral electrodes in each of the five sheaves were located within or adjacent to the caudate nucleus and the pes coronae radiatae, possibly with some extension into the lateral ventricle. The most caudal electrodes were in the lateral mesencephalic nucleus, peripeduncular nucleus, substantia nigra, pes pedunculi, medial and lateral lemniscus. The intermediate electrodes extended through the following thalamic nuclei: reticular, dorsooralis, zentrolateralis, ventrocaudalis, ventro-intermedius, ventrooralis and the medial geniculate body. There were also extensions into the internal capsule.

Twenty-seven electrodes were selected for study and each was referred to a common intrathalamic reference composed of the remaining seven electrodes. These seven, grouped towards the centre of three of the sheaves, were chosen because of a relatively low level of intrinsic and evoked activity during a preliminary series of tests. Simultaneous recording was carried out from a silver–silver chloride electrode at the scalp vertex referred to a linked pair of similar electrodes on the mastoid processes. A further pre-frontal electrode was used as a control for eye movements.

A 16-channel EEG was recorded through high gain amplifiers with input impedance of 100 Mohm and using time constants ranging from 1.2 to 5 s. On-line averaging was carried out using a PDP 12 computer. Additional averaging and analysis was undertaken off-line. Five test sessions took place from one to two weeks after implantation of the electrodes. No electrocoagulative treatment had been carried out at that stage but the patient was alert and coperative.

In the slow potential test session paired presentations of click (S_1) followed by repetitive flashes (S_2) were used. Initially the patient was required to make no motor response. Later she was asked to press a button as quickly as possible with her right hand to terminate S_2. The S_1–S_2 interstimulus interval was 1 s and a total of 128 irregularly spaced trials were carried out. Trials were averaged online in sets of eight.

Widespread slow potential changes were observed from brain-stem electrodes during the S_1–S_2 + response condition, those from the most rostral electrodes being positive with respect to the intrathalamic reference and those from the most caudal (mesencephalic) electrodes negative. The intermediate electrodes in each sheaf, those in thalamic nuclei, showed little or no slow shifts (Fig. 1). The form and duration of the slow changes from the caudal electrodes closely resembled the vertex CNV and the positive shift seen at the rostral electrodes constituted a phase reversal of the caudal response components. Amplitudes and onset latencies of the slow potential shifts observed are given in Table 1. Because of the short intrinsic time constant of gold electrodes, the amplitudes of slow shifts measured sub-cortically were probably about 20% less than the true values.

Choice of an intrathalamic reference made interpretation of the phase inversion between rostral and caudal electrodes equivocal. Six sub-cortical electrodes showing clear evidence

Table 1 Amplitude and Latency Onset of Slow Potential Shifts

Electrode location	Slow potential change	
	Amplitude (mean level for 200 ms preceding S_2)	Latency to onset
Scalp (Cz)	-9 μV	470 ms
Sub-cortical (rostral to thalamus)	$+4$ μV to $+10$ μV	340 to 360 ms
Thalamus	$+2$ μV to -3 μV	—
Mesencephalon	-5 μV to -25 μV	230 to 280 ms
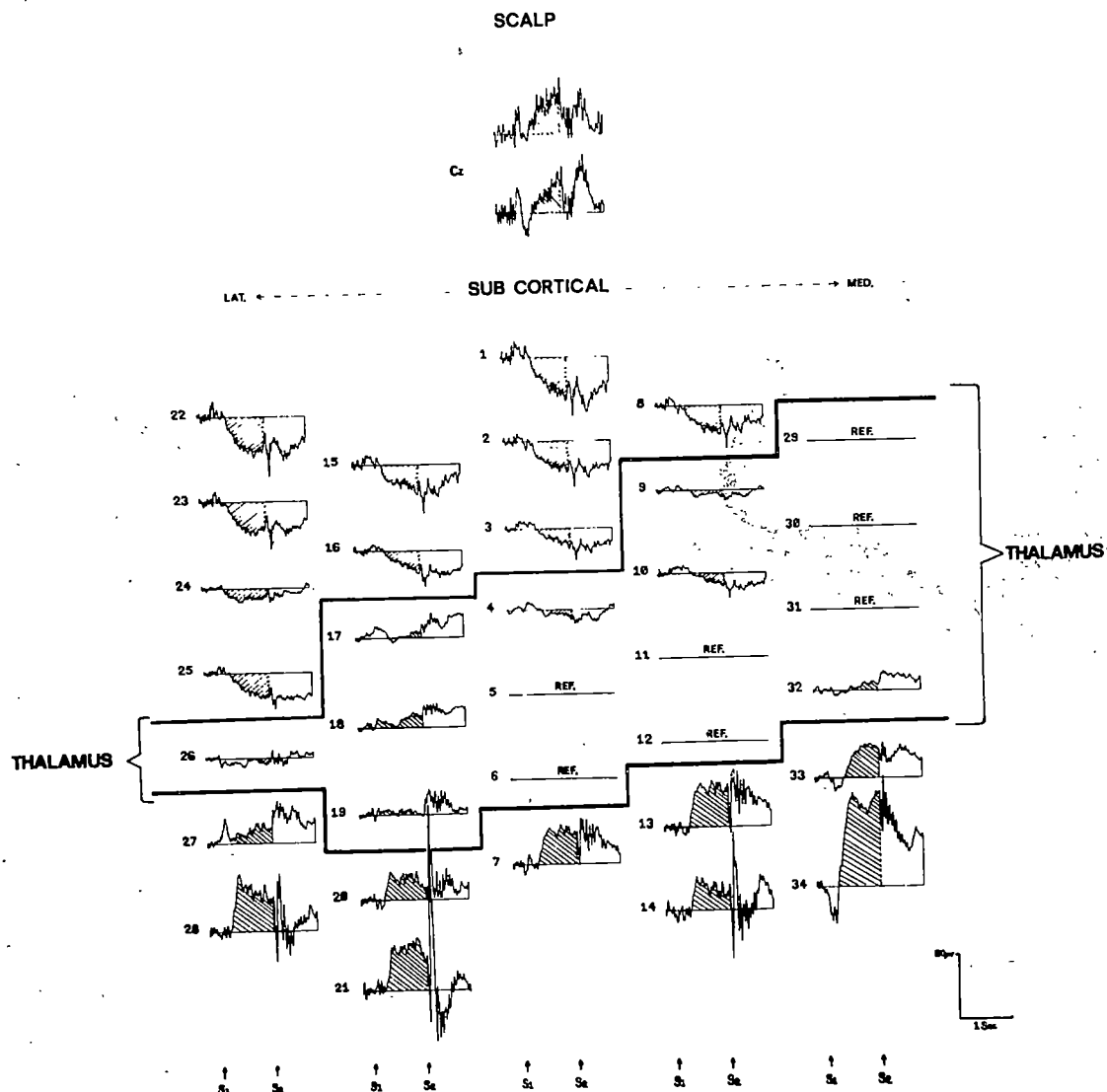
Fig. 1 Diagrammatic layout of averaged CNVs ($N=40$) recorded from the scalp and brainstem. Electrode C_z is referred to linked mastoids. Each sub-cortical electrode has a common reference composed of electrodes 5, 6, 11, 12, 29, 30, 31, selected for their low level of evoked activity. S_1 is a click, S_2 are repetitive flashes terminated by a button press. Calibration is 20 μV. There is a prominent CNV at the most caudal (midbrain) electrodes and a corresponding positive variation at the most rostral extra-thalamic electrodes.

of slow potential changes were therefore selected to conduct a comparison of the scalp and intra-thalamic references. Each electrode was referred both to the intra-thalamic reference and, on a separate channel, to the mastoid reference. The waveform and polarity of slow potential change at a given electrode was found to remain the same irrespective of whether the reference was thalamic or mastoid.

Evoked potentials to single click, flash and somato-sensory stimuli were also recorded. They showed distributions very similar to that of the CNV; the largest responses were observed from mesencephalic structures, smaller responses were seen from more rostral extra-thalamic and caudate nucleus electrodes and, in the case of flashes and clicks, there were indications of small, but consistent responses from some electrodes within the thalamus itself. The most prominent component to flash and click stimuli was a negative peak with a latency of 92 ms (or slightly later at some locations). An earlier but less prominent negative peak was seen between 42 and 48 ms after flash stimuli and at 62 ms after click stimuli. The somato-sensory stimulus, consisting of electrical stimulation of the right (ipsilateral) median nerve at the right wrist, elicited responses, principally in mesencephalic structures.

The extent to which habituation of evoked potentials could be observed in the brainstem was investigated by selecting four

electrodes, which had shown clear responses to an irregular flash, and observing their responses to similar flashes presented at regular intervals. 160 flashes were presented at intervals of 1.5 s and 80 at intervals of 1.0 s. Trials were averaged in sets of four to observe any trend towards habituation. Electrodes 14, 20 and 21, located in midbrain, showed little evidence of habituation at either interval. At electrode 1, the most rostral of the group, the principal response component observed during irregular flash stimulation had been a negative peak with a latency of 112 ms. During regular stimulus presentation at intervals of 1.5 s this component was absent on at least half of the averages. During regular presentation at the 1.0 s interval it was no longer observable.

The findings, from both patients, of CNVs in mesencephalic structures and the presence of simultaneous positive variations in more rostral extrathalamic white matter and caudate nucleus are generally consistent with those of Rebert[4] in Macaque monkeys performing a discriminative foreperiod reaction-time task. The evidence clearly implicates the diffuse and so-called non-specific projection systems of the brain in man in a situation involving the association of incoming signals. It demonstrates some aspects of the temporal relationships between subcortical and cortical processing and indicates that both long latency evoked potentials and slow potentials are

processed by essentially the same brainstem structures. Nevertheless the diversity of patterns encountered and the results of habituation suggest that these diffusely acting systems are capable of more than an undifferentiated arousal response.

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Hapten-reactive Helper Lymphocytes

SINCE the discovery of the synergism between lymphocytes derived from the thymus (T cells) and those originating in the bursa or bone marrow (B cells) in the induction of humoral antibody synthesis[1-3], numerous studies have been carried out to establish, (1) if both T and B cells show specific immunocompetence, and (2) how they express their potential competence.

Both T and B cells have a specific immunological memory[1-5], and so have been assumed to bear specific receptors for antigen. The receptors on B lymphocytes are immunoglobulins[6-8] and their specificity seems to be very similar to that of serum antibodies[6,9]. T cells also have antigen-binding receptors[10-12], but direct study of the nature of T cell receptors has met with difficulties[9]. Several attempts have therefore been made to characterize indirectly the receptor(s) according to the selective effect of various immunogens on the function of normal or primed T lymphocytes[13-15]. Contradictory results have been obtained[13-15] from studies to establish whether T and B cells carry receptors which recognize the same spectrum of antigenic specificities.

Hapten-specific B cells have been demonstrated unequivocally[6,9,16], so evidence for the existence of hapten-specific T cells will be important. Hapten-reactive T lymphocytes have been found in functional tests[17-20] and in hapten-binding assays[16]. An example of the former is the helper function of DNP-reactive (dinitrophenyl) lymphocytes from animals whose skins were painted with DNP. Cells from mice immunized with bovine serum albumin (BSA) were depleted of T cells and admixed with the DNP-reactive lymphocytes. On stimulation with DNP-BSA, an augmented anti-BSA response was obtained. The functional criteria for the helper effect being due to T cells was the demonstration that the skin-painted mice elicited strong delayed hypersensitivity to DNP[19]. Direct proof for the helper effect being ascribed to T lymphocytes is, however, still missing. The helper effect could be due to (1) T lymphocytes[17-20], (2) anti-DNP antibodies[21], or (3) anti-DNP antibody coated or "armed" macrophages[22].

To distinguish between these, cells from mice whose skins had been painted with DNP were treated as follows. (1) They were purified on anti-immunoglobulin coated columns (anti-IgM columns) which selectively retain B lymphocytes[8]. (2) They were then treated with anti-θ antiserum plus complement, which according to Raff[23] should eliminate T lymphocytes.

The advantage of using these two techniques in parallel is that the column separation also eliminates cells with cytophilic, surface, adherent anti-DNP antibodies, whereas the anti-θ treatment might not. The experimental design used was similar to that described by Mitchison[18]. Mice were immunized with 200 μg BSA in Freund's complete adjuvant (CFA), and BSA immune spleen and lymph node cells were collected from these animals 1-3 months later. Some of the cells were treated in vitro with anti-θ antiserum plus complement[9] to eliminate BSA-specific T cells, which will be called B anti-BSA cells. Other mice had their skin painted with dinitrofluorbenzene (DNPF) 6-7 days before transfer or were immunized with DNP₆MSA (mouse serum albumin) or DNP₇OA (ovalbumin) 3-6 weeks before transfer. Cells from these animals were used either untreated, after passage through an anti-IgM column or after anti-θ plus complement treatment. These will be called helper cells. B anti-BSA and helper anti-DNP

Table 1 DNP-reactive Helper Lymphocytes

Group No.	B cells *	Anti-θ †	Helper cells ‡	Column§	Antigen‖	Anti-BSA antibodies¶ Log₂ titre	Log₁₀ABC
1	10⁷ BSA	−	−	−	DNP₅BSA	11.7 ± 1.25	2.84 ± 0.13
2	10⁷ BSA	+	2 × 10⁷ NC	−	DNP₅BSA	4.8 ± 0.94	0.76 ± 0.23
3	10⁷ BSA	+	2 × 10⁷ DNP-Skp	−	DNP₅BSA	7.1 ± 0.54	1.19 ± 0.15
4	10⁷ BSA	+	2 × 10⁷ DNP-Skp	+	DNP₅BSA	8.2 ± 1.02	1.77 ± 0.18
5	10⁷ BSA	+	2 × 10⁷ DNP₆MSA	−	DNP₅BSA	7.1 ± 0.67	1.54 ± 0.14
6	10⁷ BSA	+	2 × 10⁷ DNP₆MSA	+	DNP₅BSA	7.9 ± 1.02	2.10 ± 0.22
7	10⁷ BSA	−	−	−	−	3.2 ± 0.71	0.69 ± 0.17
8	—	−	2 × 10⁷ DNP-Skp	−	DNP₅BSA	0.2 ± 0.49	Neg.

* B cells, mixed spleen and lymph node cells from CBA × Balb/c mice immunized 8 weeks before transfer.
† −, BSA immune cells treated with complement only (guinea-pig serum diluted 1 : 4 in BSS); +, BSA immune cells treated with anti-θ antiserum plus complement[9].
‡ Helper cells: NC = normal lymph node cells; DNP-Skp = cells from mice painted with 500 μg DNPF 7 days before transfer. DNP₆MSA = mixed spleen and lymph node cells from DNP₆MSA immune mice (3 week immune).
§ −, Non-passed cells; +, cells passed through an anti-IgM coated column. (% θ positive cells: DNP-Skp-C = 65; DNP₆MSA-C = 49; DNP-Skp-P = 93; DNP₆MSA-P = 89.)
‖ Antigen (10 μg) given together with the cells.
¶ Log₂ titre, log₂ haemagglutination titre against DNP₇OA-SRBC (2-ME resistant titre ± one s.d.); ABC, antigen binding capacity at 0.001 μg BSA : ¹²⁵I/ml. ± one s.e.

Table 2 DNP-reactive Helper T Lymphocytes

Group No.	B cells *	Helper cells †	Column ‡	Anti-θ §	Antigen‖	Anti-BSA antibodies¶ Log₂ titre	Log₁₀ABC
1	5×10^6 BSA	2×10^7 NC	−	−	DNP_5BSA	5.2 ± 0.51	0.20 ± 0.14
2	5×10^6 BSA	3×10^7 DNP-Skp	−	−	DNP_5BSA	8.9 ± 1.02	1.48 ± 0.09
3	5×10^6 BSA	1×10^7 DNP-Skp	−	−	DNP_5BSA	7.2 ± 0.51	0.75 ± 0.07
4	5×10^6 BSA	3×10^7 DNP-Skp	+	−	DNP_5BSA	10.4 ± 1.33	1.76 ± 0.13
5	5×10^6 BSA	1×10^7 DNP-Skp	+	−	DNP_5BSA	9.1 ± 1.26	1.41 ± 0.13
6	5×10^6 BSA	3×10^7 DNP-Skp	−	+	DNP_5BSA	4.5 ± 0.89	0.16 ± 0.25
7	5×10^6 BSA	1×10^7 DNP-Skp	−	+	DNP_5BSA	4.7 ± 0.81	0.38 ± 0.24
8	5×10^6 BSA	2×10^7 NC	−	−	$Sulph_5BSA$	5.2 ± 0.68	0.24 ± 0.19
9	5×10^6 BSA	2×10^7 DNP-Skp	−	−	$Sulph_5BSA$	5.1 ± 1.02	0.57 ± 0.22
10	5×10^6 BSA	−	−	−	−	5.0 ± 1.14	0.44 ± 0.29
11	5×10^6 NC	2×10^7 DNP-Skp	−	−	DNP_5BSA	0.8 ± 0.51	Neg.

* Spleen cells from CBA × Balb/c mice immunized 12 weeks before transfer. They were treated with anti-θ antiserum plus complement[9].
† NC, Normal lymph node cells; DNP-Skp = see Table 1.
‡ −, Non-passed cells; +, cells passed through an anti-IgM coated column. (% θ positive cells: DNP-Skp-C=69%, anti-MIg passed =97%.)
§ −, Non-treated; +, anti-θ treated (number of anti-θ treated cells was adjusted so that the given numbers of live cells were transferred).
‖ Antigen (10 μg) given together with the cells.
¶ See Table 1.

cell populations were mixed *in vitro* and injected together with DNP_5BSA (or with $Sulph_5BSA$ = sulphanylated BSA as specific control) into sublethally irradiated syngeneic recipient mice (500 R). The mice were bled 10 days later. Individual antisera were tested for anti-BSA antibodies by haemagglutination[9] and by a modified Farr assay[24].

A representative experiment showing the impact of anti-MIg columns on the helper effect of lymph node cells from (DNP-Skp) mice whose skins had been painted with DNP and from DNP-MSA immune mice can be seen in Table 1. Both control and anti-IgM column passed DNP-reactive lymphocytes were very active as "helpers", the latter cells being the most active[8]. The same result was obtained in three more similar experiments. In one of these DNP-OA immune cells were used instead of DNP-MSA immune cells. Again, either control or anti-IgM column passed cells functioned as "helpers". The anti-IgM column passed cells were tested for DNP-specific rosette-forming cells[9] (RFC) before and after passage. The figures for the experiment in Table 1 were: before passage; DNP-Skp = 2,750 ± 298 RFC/10^6 lymphoid cells (± one s.d.), DNP-MSA cells = 7,890 ± 305 RFC/10^6 cells: after passage; DNP-Skp = 90 ± 85 RFC/10^6 cells and DNP-MSA cells = 105 ± 75 RFC/10^6 cells. In summary these results indicate (1) that the helper cell belongs to the class of lymphocytes having very little if any conventional immunoglobulin on their surface (T cells) and (2) that removal of B cells and free or cell-bound anti-DNP antibodies had no impact on the helper function observed.

Table 2 shows an experiment where (1) the effect of anti-IgM column passage, (2) the effect of anti-θ antiserum plus complement and (3) the specificity of cells from mice painted with DNP was tested using two different doses of helper cells. As in Table 1, anti-IgM column passage increased the helper capacity of DNP-reactive lymphocytes; treatment with anti-θ antiserum plus complement abolished the helper capacity; and the helper effect observed was specific. Two more experiments proved the abolishing effect of anti-θ antiserum plus complement on DNP-reactive helper cells. In summary, these experiments demonstrate the existence of the hapten-specific helper effect of T lymphocytes.

Other studies in this laboratory have failed to demonstrate a helper effect of anti-hapten antibodies[21] or antibodies directed against the new antigenic determinants introduced in MSA by the haptenic coupling (Rubin, unpublished). Help by antibodies was, however, found in a similar system in the rabbit[25]. The failure of others[21] to demonstrate DNP-specific helper cells might be due to (1) the dose of DNPF applied (500 μg DNPF seemed to be optimal in our system), (2) the time between immunization and collection of immune cells[26],

and (3) the number of cells used. Five out of six experiments have shown that in order to get a significant helper effect, 2×10^7 DNP-reactive cells or more were needed (exception, Table 2). Cell dilution studies with BSA-immune and DNP-reactive cells, unpassed or anti-IgM column passed, have shown that whereas 2×10^7 DNP reactive cells are needed for a significant helper function, only 10^6 BSA immune (anti-IgM passed) or 5×10^6 unpassed BSA immune cells are needed for a significant BSA helper function (Rubin and Wigzell, unpublished).

Whether the DNP-reactive T lymphocytes demonstrated in this paper show the same specificity as humoral anti-DNP antibodies and anti-DNP B lymphocytes is still unknown. Studies using DNP-BSA conjugates with DNP coupled to BSA by different procedures to induce different new antigenic determinants in the BSA molecule (Rubin and Aasted, unpublished results) might solve this problem.

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Chimaeras and the Forbidden-clone Theory of Self-tolerance

THE forbidden-clone theory of self-tolerance, which postulates that if immunologically competent cells capable of anti-self reaction arise they are soon eliminated, was widely accepted for a long time[1-3], but it has recently been challenged[4-6]. Part of the challenge rests on the demonstration that a factor capable of blocking anti-self reaction is present in the serum, and part on *in vitro* studies indicating that cells capable of anti-self reaction occur in mice and rats. The studies with mice used chimaeras, also known as allophenic or tetraparental mice, which are made by fusing morulae of different genotypes. It is probably too early to say whether the forbidden-clone theory has been dethroned, but it may be pointed out that the studies with chimaeras are open to objection. As chimaeras may again be used for work of this nature, this objection is perhaps worth stating.

It is based on the fact that the two types of cells in a chimaera are not uniformly mixed throughout, and the mixture is generally far from intimate. Our examination of 10 chimaeras made from pigmented and unpigmented genotypes, all showing a good mixture of the two types of pigment cells in the fur, revealed that not only were large parts of the pigmentary layer of the retina of one kind or the other, but one retina was wholly pigmented, one almost wholly pigmented, and three almost wholly unpigmented[7]. The distribution of the migratory pigment cells in the iris, choroid and inner ear was similarly uneven[8]. To obtain a clearer picture, I examined the Harderian gland in the same animals. This is a large, thick structure, which almost surrounds the medial half of the eye, and is extremely rich in melanocytes. Two glands (in different animals) had no pigmented cells at all, and three had large parts that were entirely unpigmented. For obvious reasons it is impossible to say whether any gland was colonized solely by pigmented cells, but it is reasonable to assume that a comparable number might have been, the histological appearance of some being consistent with this assumption. Taking the entire cranial region, two chimaeras were unilaterally lacking in pigmented melanocytes of the migratory type, and one or two presumably in unpigmented ones.

If the chimaeras can be so wanting in uniformity in regard to pigment cells of both types, they may well have large regions in the thymus that are of single origin. An appreciable proportion of lymphocytes would then be expected to acquire their specificity in a region of their own genotype, and so be capable of reacting against cells of the other type. As the formation of lymphocytes is believed to be a continuous process, such cells would be found in the lymph nodes of chimaeras at all times, and their presence would not by itself rule out the mechanism implicit in the forbidden-clone theory as an additional factor in self-tolerance.

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Dislocations in Tobacco Mosaic Virus

I DO not allege that the way Butler and Klug use "dislocation" is incorrect. I merely point out that as crystal dislocations occur in tobacco mosaic virus (TMV) and may perform important functions, "confusion is bound to arise if the term dislocation continues to be used loosely". Confusion is even more likely when the term is used in the same context by the same group in both strict ("screw dislocation"[1]) and loose (for example on p. 133 of ref. 2, "step dislocation at the end of the single helical rod") senses.

Butler and Klug deny my statement that members of their group refer to helical forms being dislocated or containing a dislocation. The second quotation above is sufficient to show their denial is false. I can supply a corroboratory quotation from every source I cite.

There is nothing wrong with taking the disk as the reference — I find a different reference more convenient. My reference is similar to Klug's radial projection[3], which he and his coworkers use elsewhere but not here.

Just as Butler and Klug found it necessary or convenient to present detailed models "to give some general feel for the process", so have I. Without detailed models an explanation would be difficult if not impossible. What may appear to them "differences in detail" are in fact important differences: as I explain, one of their mechanisms converts the disk directly to a portion of a helix with the same number of subunits per turn as in the completed virion whereas the other requires an additional step.

My mechanisms, based on theirs, depend no more on "continuity of the disk" than do theirs. Just because subunits can be gained or lost in no way rules out dislocations. On the contrary, a very important mode of movement of dislocations requires the loss or gain of subunits[4]. It is similar to the mechanism of climb that I describe.

In their final paragraph Butler and Klug express an opinion which I am confident will be proved wrong. What can be stated with certainty is that dislocations are present in many types of biological structures. The bibliography on dislocations in biological structures which I am compiling already contains more than a hundred references.

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SV40 Protection in Myeloma Oncogenesis

SIMIAN virus SV40, a DNA tumour virus, causes a productive infection in both monkey and human cells, leading to lysis of the cells and release of infectious virus. In murine systems, however, the virus transforms the cells, leading to new virus-specific antigens on the transformed cells[1]. These transformed cells induce tumours in mice which then respond to the tumour specific antigen[2,3]. I report here protection of mice by SV40 when given with syngeneic myeloma tumour cells.

The myeloma line X5563, syngeneic for C$_3$H mice, was obtained from Dr M. Potter of the National Institutes of Health and has been maintained here in vitro. SV40 (obtained from Dr P. Naha of Mill Hill) was grown on BSC-1 cells, and titred 10^8 plaque-forming units (PFU) ml.$^{-1}$. The virus was inactivated 1 h in some studies, using a Hanovia germicidal lamp 14 cm away. Significance was tested using the Newman Keuls method of multiple comparison.

In the first experiment, groups of 50 C$_3$H female mice were inoculated i.p. with 1.5 ×10^6 viable cells in: (1) 0.2 ml. of tissue culture medium; (2) 0.2 ml. of active SV40; or (3) 0.2 ml. of ultraviolet-inactivated SV40. A fourth group received 0.2 ml. SV40 as an additional control. As seen in Fig. 1, deaths in the control group were first observed on day 48, and by day 57, 67% of the mice were dead. By contrast, in the group given myeloma and active SV40, deaths were first seen on day 55. Similarly, in the group given myeloma and inactivated virus, deaths were first observed on day 59. In both virus-treated groups, the mortality was significantly lower ($P<0.05$) than the controls. Mice inoculated with SV40 had no evidence of tumour when killed 73 days after inoculation.

Fig. 2   a, Mice were inoculated i.p. with 1.5 × 10^6 myeloma cells on day 0 (●), 1.5 × 10^6 myeloma cells on day 0, 0.4 ml. of SV40 on day 2 (■), or 1.5 × 10^6 myeloma cells on day 0, 0.4 ml. of SV40 on day 13 (▲). b, Mice were inoculated i.p. with 1.5 × 10^6 myeloma cells on day 2 (●), 0.4 ml. of inactivated SV40 on day 0, 1.5 × 10^6 myeloma cells on day 2 (■), or 0.4 ml. of active SV40 on day 0, 1.5 × 10^6 myeloma cells on day 2 (▲). c, Mice were inoculated i.p. with 1.5 × 10^6 myeloma cells on day 13 (●), 0.4 ml. of active SV40 on day 0, 1.5 × 10^6 myeloma cells on day 13 (■), or 0.4 ml. of inactivated SV40 on day 0, 1.5 × 10^6 myeloma cells on day 13 (----). In all cases animals were observed daily and deaths recorded.

Fig. 1   Mice were inoculated i.p. with 7 × 10^5 myeloma cells (●), 7 × 10^5 myeloma cells in 0.2 ml. active SV40 (★), 7 × 10^5 myeloma cells in 0.2 ml. of inactive SV40 (▲), or 0.4 ml. of SV40 (----) on day 0. The animals were observed daily and deaths recorded.

To exclude the possibility that protection was conferred by factors from the BSC-1 (monkey) cells, on which SV40 was grown, mice were inoculated with 1.5 × 10^6 viable X5563 cells in 0.2 ml. BSC-1 conditioned medium. Myeloma cells were also inoculated with NIP-T4 phage (courtesy of Dr A. Cross) to determine if the presence of another viral antigen could confer the same protection seen with SV40. Neither groups was significantly protected against the myeloma cells. To exclude the possibility that SV40 lysed the cells, thus effectively lowering the number of cells given to the animal, 2 × 10^7 PFU SV40 was added to 1.5 × 10^6 cells in 0.2 ml. After 2 h the cells were washed and grown in vitro. There was no evidence of lysis.

Protection has been demonstrated in the above experiment when virus was given simultaneously with the tumour cell. In the following experiments, virus was given either before or after myeloma challenge to ascertain whether protection was achieved. Groups of 25 C$_3$H mice were inoculated with 1.5 × 10^6

viable tumour cells. One group received virus 2 days later, and the second group 13 days later. As seen in Fig. 2a, the groups treated with virus were significantly protected ($P<0.001$). In the second experiment (Fig. 2b), groups of mice were pretreated with either active or inactive virus, and two days later, challenged with 1.5 × 10^6 tumour cells. Again, protection in the latter groups was significant ($P<0.001$). In the final experiment (Fig. 2c), mice were pretreated with active or inactive SV40,

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and inoculated with tumour cells 13 days later. Although preinoculating mice with active virus delayed the onset of death, the most significant protection was achieved when mice were pretreated with inactive virus. In this group, no animals died up to 75 days after inoculation.

These results show that SV40 protects mice against a tumour challenge of syngeneic myeloma cells. The protection occurring when the virus was given simultaneously with the tumour could be explained by adsorption of virus to the tumour cell surface, thus altering the antigenicity of the cell. It is more difficult to explain how the virus can protect when given up to 13 days before or after myeloma challenge; perhaps SV40 "homes in" on the cells *in vivo*. There is no evidence, based on the *in vitro* observations, that the cells are lysed. Why ultraviolet-inactivated virus should be more effective than live virus in protecting the host is still unclear. It is possible, based on work demonstrating *in vitro* repair of ultraviolet-damaged SV40 (ref. 4), that repair might have occurred *in vivo*, the virus thus becoming a source of new and varied antigen. Further studies are underway to elucidate the mechanism of SV40 protection.

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Depression of Immune Response to Moloney Leukaemia Virus by Malarial Infection

MALARIAL infection depresses the immune response to a variety of antigens in mice[1-6] and man[7,8]. It has been postulated that malarial immunodepression is implicated in the development of a human neoplasm, Burkitt's lymphoma[9], the geographical distribution of which coincides with that of holoendemic malaria[10]. In Swiss mice, malarial infection has been shown to increase the rate of spontaneous lymphomagenesis[11]; and in adult Balb/c mice to potentiate the induction of lymphomas by the Moloney leukaemia virus, MLV (ref. 12). Here we present evidence that the latter effect is accompanied by a reduction in the detectable levels of circulating neutralizing antibody to MLV, and in particular by the absence of IgG neutralizing antibody.

Three groups of fifteen Balb/c female mice aged 9 weeks were infected with *Plasmodium berghei yoelii* (Pby) only, MLV alone, or both agents together, as previously described[12]; a fourth group was untreated. The onset of lymphoma is illustrated in Fig. 1. All surviving mice were bled at intervals from 2.5 weeks to 28 weeks after infection, and pooled sera from each group were tested for virus-neutralizing activity (Fig. 2) by inhibition of focus formation by the MLV pseudotype of the Harvey strain of murine sarcoma virus MSV (MLV) (ref. 13). In the group infected with MLV and Pby the neutrali-
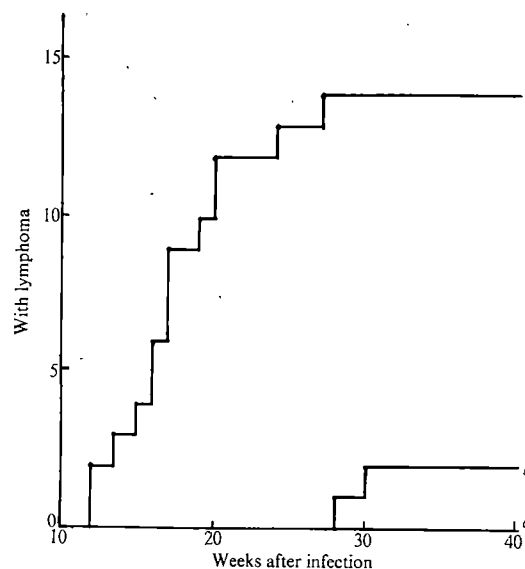
Fig. 1 The number of mice developing lymphoma after infection with MLV alone or MLV and Pby. *a*, Pby alone (0/15); *b*, MLV only (2/15); *c*, Pby+MLV (14/15).

zing antibody response 3.5 weeks after infection did not differ from that of mice infected with MLV alone, but thereafter remained consistently lower. Also included in Fig. 2 are neutralizing antibody levels from a group of mice infected with MLV as neonates. Eight weeks after infection the level of antibody observed in these animals was similar to that in mice infected with Pby and MLV as adults, but at 10 weeks the mice that had been inoculated neonatally became leukaemic and antibody was no longer detectable in their sera. Neutralizing activity had also disappeared from the sera, taken at 12 weeks, of individual leukaemic mice from the group infected
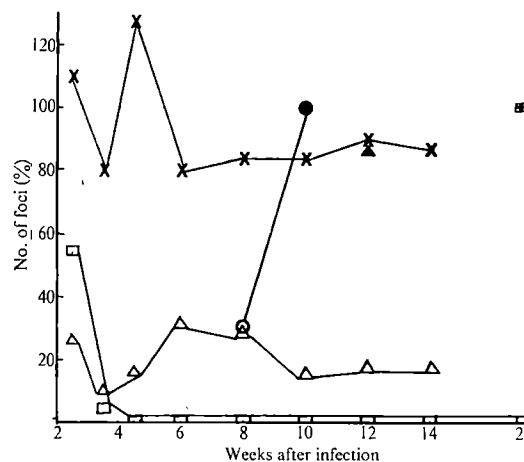
Fig. 2 Percentage reduction of focus formation by MSV (MLV) by sera from Balb/c mice. ×, Infected with Pby alone; □, with MLV alone; △, with both MLV and Pby; ○, with MLV alone as newborns. ■, ▲, ●, Sera from leukaemic mice. In each test 0.02 ml. of heat inactivated (56° C, 30 min) serum was added to 0.18 ml. of a pool of the Harvey strain of MSV containing about 100 focus forming units. The mixture was incubated at room temperature for 90 min, 3.4 ml. of medium (Dulbecco's modification of Eagle's medium with 5% heat-inactivated calf serum) was added and 1.2 ml. aliquots were transferred to each of three 50 mm Nunclon dishes seeded the previous day with 2×10^5 Balb/c 3T3 cells (on which focus formation of MSV follows one-hit kinetics)[13] and treated with 5 ml. of DEAE-dextran[22] at 30 μg ml.$^{-1}$ in phosphate-buffered saline for 1 h at room temperature immediately before infection. The dishes were incubated at 37° C. One day later 4 ml. of medium were added. Seven days after infection the dishes were stained (Giemsa) and foci counted.

Fig. 3 Titration of sera from Balb/c mice at 6 weeks after infection (*a* and *b*) and at 10 weeks (*c* and *d*). With 2ME treatment (*b* and *d*) or without (*a* and *c*). Sera were mixed with an equal volume of saline, or saline containing 0.2 M 2ME, left for 1 h at room temperature and dialysed overnight at 4° C against 400 ml. of saline. ×, Uninfected mice; ■, MLV only; △, MLV+ Pby. The vertical lines indicate the variation of focus number between two replicate dishes.
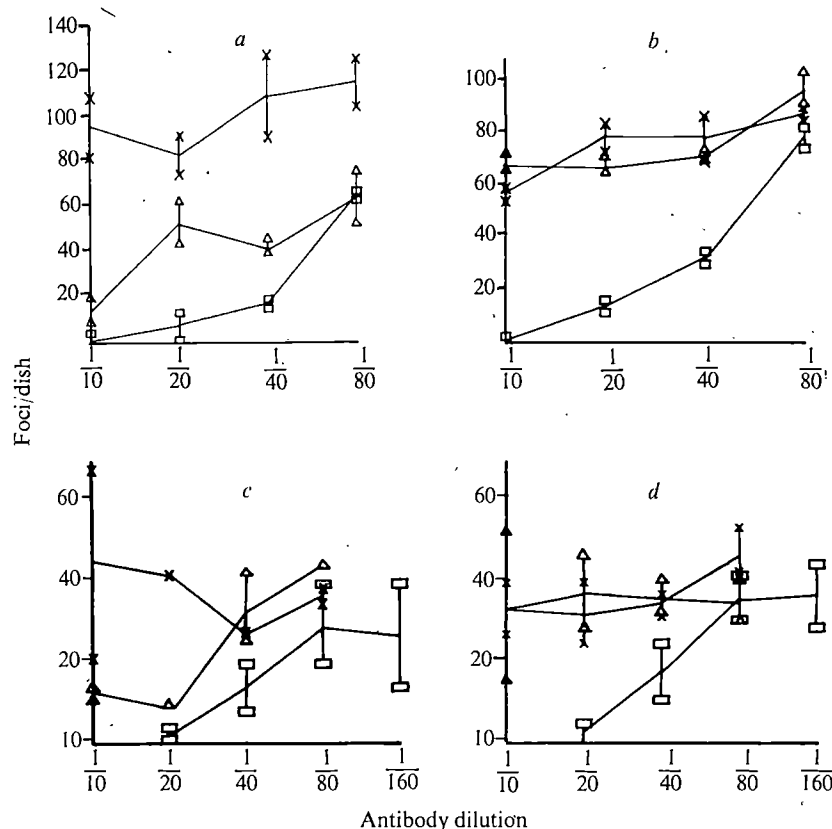
as adults with both agents, and from the serum, taken at 28 weeks, of one mouse infected with MLV only, as indicated by the solid symbols in Fig. 2.

The lack of effect of Pby infection on the early antibody response to MLV and its subsequent inhibitory effects, together with the fact that the IgG response to sheep erythrocytes is depressed more severely than the IgM (H. S. Micklem, personal communication) suggested that Pby infection might selectively inhibit the IgG response to the virus. Also it has been proposed that the IgG response to MLV is absent in neonatally-infected mice, where infectious circulating immune complexes have been found, neutralizable by anti-IgM but not by anti-IgG antibody[14].

Aliquots of sera from untreated, MLV infected, and Pby + MLV infected mice taken at 6 and 10 weeks after infection were treated with 2-mercaptoethanol (2ME) and neutralizing activity titrated (Fig. 3). At both 6 and 10 weeks the activity of sera from mice infected with both agents was abolished by 2ME; serum from mice infected with MLV alone was partly resistant at 6 weeks and completely resistant at 10 weeks.

The absence of measurable virus-neutralizing IgG in doubly infected mice does not necessarily mean that no such antibody is produced; we cannot exclude the possibility that the IgG is being selectively adsorbed out by virus antigens, or rapidly catabolized as a consequence of overall raised IgG levels after malarial infection[15,16]. But the absence of IgG could be accounted for if malarial infection were specifically preventing T (thymus-derived) lymphocytes from responding to MLV, because for several antigens it has been shown that the IgG response is more T cell-dependent than the IgM response[17,18].

The depressed humoral response to MLV in dually-infected mice could contribute to the enhancement of lymphomagenesis. The importance of antibody in controlling lymphomagenesis by MLV has been demonstrated by conferring protection in passive antibody transfer experiments[19]. ALS treatment enhances lymphomagenesis by MLV (ref. 20), and reduces the levels of detectable circulating neutralizing antibody[21]. We cannot judge whether the absence of IgG could be of particular significance in allowing malignant cells to escape immune attack.

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A Critique of McClare's Quantum Mechanical Muscle Model

THE explanation of muscle contraction by McClare[1,2] is at variance with the current tenets of molecular spectroscopy. Lifetime measurements have shown that, in most cases, the excimer has a shorter half-life than that of the parent monomer[3]. In pyrene, the example quoted by McClare, the half-life (at room temperature) of the monomer is 31×10^{-8} s, while that of the excimer is only 4.4×10^{-8} s.

Azumi and McGlynn[4] observed an excimer emission from solid solutions of pyrene with a lifetime of 10^{-2} s, which they attributed to "an inherent forbidden character of excimer fluorescence itself". It was later found[5] that their delayed fluorescence arose from an excimer produced by triplet-triplet annihilation; that is, the emission owed its longevity to the delay in the production of the emitting species and not to its slow decay.

I have shown[6] that two molecules in the lowest triplet state will not interact to yield an excited singlet species (monomer or excimer) if they are situated 3.0 nm apart. Thus McClare's oscillators, even if they are postulated to be in the first excited triplet state, would not interact and come closer. If the initial distance is changed to 1.0 nm, electron exchange interaction leading first to an excited singlet monomer and later to an excimer will occur; but then the excimer will not be long-lived. If the excimer has a centre of symmetry, excimer fluorescence will be dipole-forbidden[7]. Experimental evidence, however, suggests that random thermal motion of the two monomers can lower the symmetry and make the transition dipole-allowed. In a rigid matrix, a symmetrical excimer, once formed, will be unable to radiate; but in such a matrix the two oscillators will be prevented from coming closer and McClare's model would fail.

McClare also presents the analogy of the lowest triplet state of chrysene which can be stabilized for as long as a second, and argues that an excimer could also be similarly stabilized. Although the radiative transition of a symmetrical excimer is dipole-forbidden, as is the phosphorescence from the triplet state of an organic molecule, there is an essential difference between the two species. The first triplet state is the lowest excited state of the molecule, but the singlet excimer state is not; the excimer can always decay by crossing over to its (lower lying) triplet state. Hence a symmetrical excimer cannot be stabilized for as long as the lowest triplet state of an organic molecule.

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McClare's Quantum Mechanical Muscle Model

STARTING from the belief that the "energy" for muscular contraction is derived from the "energy" released by the hydrolysis of ATP, McClare[1] has concluded that this "energy" must initially be stored in individual molecules of ATP. The amount of "energy" so stored is supposed to equal the enthalpy change for the hydrolysis of ATP (presumably in its ground state), at *p*H 7.4. A considerable part of the quoted figure (-40 kJ mol^{-1}) is, in fact, due to the heat of neutralization of a proton which is formed in near stoichiometric amount at this *p*H (refs. 2, 3). Nevertheless, McClare proposes that the total enthalpy change is somehow trapped in the other two products of hydrolysis, ADP and inorganic phosphate, which subsequently exist in an excited "state", out of thermal equilibrium with surrounding molecules for a significant time. A calculation then shows that the wavelength of radiation having energy equivalent to this enthalpy change is 3 µm, which lies in the infrared. McClare concludes from this that the "energy" is stored (in ADP and inorganic phosphate) in a vibrational mode. The lifetime of a vibrational excited state is quoted as being *ca.* 10^{-7} s.

But this figure is typical only for dilute gases of small molecules (2 to 6 atom at 10^{-2}–10^{-3} atm) where the lifetime is collisionally limited. At much lower pressures (for example, in outer space), the lifetime of a single vibrationally excited molecule is its radiative lifetime, which for ordinary molecules is of the order of 10^{-4} s. Under such conditions, the excited energy-level is sharp, with a linewidth of about 5×10^{-8} cm^{-1}. In aqueous media, on the other hand, vibrational energy-levels as revealed by infrared absorption bands are rather broad (typically $\Delta\bar{\nu} = 100$ cm^{-1}) and the lifetimes of the vibrational excited "states" are correspondingly smaller, by perhaps about 10 orders of magnitude. This may be simply seen as follows. In a condensed phase, initially formed vibrational excited "states" are coupled intra- and intermolecularly (by "resonant transfer" in McClare's terminology) to a quasi-continuum of other vibrational "states". A quantum-mechanical treatment of uniform coupling[4-7] gives the first order decay lifetime of an initially excited zeroth-order "state" as $\tau = 5.3 \times 10^{-12} \times (\Delta\bar{\nu})^{-1}$ s ($\tau \times \Delta\bar{\nu} = \hbar/hc$). With $\Delta\bar{\nu} = 100$ cm^{-1}, $\tau = 5 \times 10^{-14}$ s; that is, 6 or 7 orders of magnitude less than the figure given by McClare. Another indication of such short vibrational lifetimes comes from, for example, the feasibility of dye lasers which otherwise would not work.

This means that for all practical purposes vibrational energies of molecules in aqueous solution are accurately distributed according to the Boltzmann Law, that is, they are thermally equilibrated. It is not possible to isolate a vibrational mode from thermal equilibrium for the time required by McClare. Even if the hydrolysis of ATP takes place on the surface of elements of the myofibril system and not in free solution the situation is unlikely to be very different. In any case, the value of the enthalpy-change would then be unknown and might well be close to zero if a proton were not produced in near stoichiometric amount.

McClare is led to "restate" the second law because of his initial premise that ATP can store and provide "energy" while remaining in steady state. The model for muscle contraction which follows requires the isolation of a particular vibrational mode from thermal equilibrium in a condensed phase, and this is not physically possible—unless, of course, Maxwell's Demon intervenes. We note that he has accused a number of muscle physiologists of invoking the assistance of this particular entity.

There can be little doubt that the behaviour of biological systems conforms to the laws of classical thermodynamics as usually understood. There is in principle no particular difficulty in calculating the value of the change in Gibbs function for a muscle contraction providing that the concentrations of all those chemical species which show a net change in amount can be measured before and after contraction. In practice this is obviously technically difficult. But no one has reported a positive value for the change in Gibbs function in these circumstances and until they do we can continue to believe that muscle contraction conforms to the second law.

Were the opening sentence of McClare's article true, that is, if the physiology, biochemistry and structure of muscle were now well understood, there would be no need for models at all. The fact is that the molecular events associated with muscle

contraction are not yet understood. While it is obviously important that, until they are, models should be proposed and considered, we conclude that the one put forward by McClare has nothing particularly to do with quantum mechanics or thermodynamics or muscle contraction.

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Hyperfiltration Streaming Potential as a Probe of Water Structure in Membranes

ONE of the most important problems in the physical chemistry of biological systems involves the question of water structure in the vicinity of a charged surface, such as a polyelectrolyte membrane. In a recent review of water structure in biological systems, Dröst-Hansen[1] has contended that a wide variety of data[2-4] point to the existence of transitions in water structure at 15° C, 32° C and 45° C, if the water is in contact with a structuring interface. We present further evidence to support the existence of a transition in the vicinity of 32°–40° C.

We have previously demonstrated that measurements of streaming potential on polyelectrolyte membranes as a function of pressure during a hyperfiltration experiment[5] yield the electro-osmotic coefficient, β. This coefficient directly measures the association between the counter-ions and the water in the membrane, and it therefore seems reasonable to believe that it should be quite sensitive to any change in water structure as a function of temperature.

Reports[6,7] of electro-osmotic experiments at various temperatures have found that the electro-osmotic coefficient tends to decrease with increasing temperature. However, McHardy et al.[8] studied 'Zeo-Karb 315', a commercial cation exchanger, from 15° C to 35° C and found no variation (all results within 2% of one another). The choice of temperature range will be shown to be unfortunate, although the results are in agreement with those observed in the present communication.

In Fig. 1, measurements of the streaming potential at various temperatures are shown as a function of the effective pressure[5] (which to a first approximation is the pressure applied). All the measurements were performed on Collodion/polyvinylamine anion exchange membranes using 10^{-2} N KCl feed solutions as previously described[9], in which the temperature was controlled to $\pm 0.1°$ C. The slope of the plots in Fig. 1 is the electro-osmotic coefficient, β, and this parameter declines substantially as the temperature is raised. When β is plotted as a function of temperature (Fig. 2), it becomes clear that the onset of a precipitous decline begins in the vicinity 35°–36° C. As mentioned earlier, the present results agree with those of
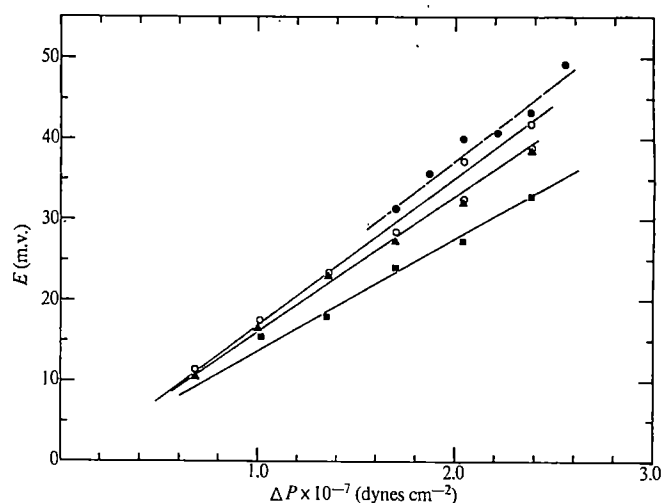
Fig. 1   Streaming potential of membrane PVA-1 as a function of applied pressure at a number of temperatures. All potentials have been corrected for the effect of pressure on the Ag/Ag Cl electrodes. ●, 291 K;   ○, 308 K; ▲, 313 K;   ■, 318 K.

McHardy et al.[8], in that β does not change by more than about 2% in the plateau region of 15°–35° C in Fig. 2.

One must now consider whether factors other than a change in water structure could produce the effect on β observed in Fig. 2. We have previously derived[5] an equation which was shown to correctly predict the concentration dependence of the electro-osmotic coefficient,

$$\beta = \frac{\varphi_w}{X + \dfrac{f_{wm}\bar{c}_w}{f_{1w}}\left(1 + \dfrac{\bar{c}_s}{t_1 X}\right)} \qquad (1)$$

where φ_w is the fractional membrane water content, X the effective charge density, f_{wm}, f_{1w} the water/membrane and anion/water frictions respectively, $\bar{c}_s$, $\bar{c}_w$ the salt and water concentrations respectively within the membrane, and t_1 is the counter-ion transport number, taken as the ratio of the counter-ion mobility to that of the salt.
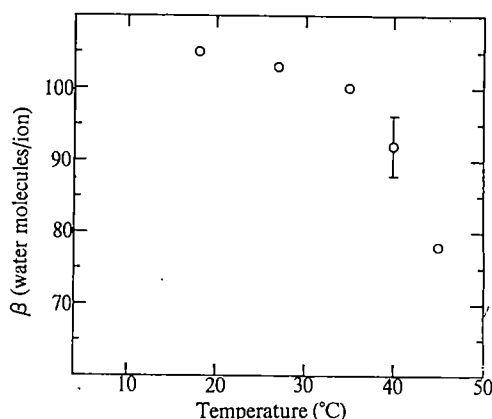
Fig. 2   The electro-osmotic coefficient as a function of temperature.

Inspection of the parameters in equation (1) reveals that either a decrease in φ_w or an increase in $\bar{c}_s$ would cause β to decline. One of the advantages of the method is that the limiting salt rejection, $\mathcal{R}_\infty$, can be measured simultaneously, and this may be used as a monitor of $\bar{c}_s$ with temperature. If $\bar{c}_s$ were to increase, one would expect $\mathcal{R}_\infty$ to decline. In Table 1, measurements of $\mathcal{R}_\infty$ and φ_w are shown at various temperatures,

and both may be seen to remain constant or perhaps increase slightly. Thus, it seems reasonable to suggest that the weak de-coupling of the outer water associated with the ion (Fig. 2) is associated with a minor change in the water structure within the membrane.

Table 1 Measurements of R_∞ and ϕ_w at Various Temperatures

Temperature	Rejection (%)	ϕ_w
25° C	58.5	0.54
30	60.5	—
35	60.0	—
40	60.0	—
45	—	0.59

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Parthenogenesis in the Mouse

In vitro treatment of mouse eggs with hyaluronidase can activate them to develop parthenogenetically as well as denuding them of cumulus cells[1-4]. Activation and subsequent behaviour of the eggs depend on certain defined conditions. Szollosi[5] observed morphological changes in unfertilized mouse eggs *in vivo* after approximately 14 h in the oviduct. Rotation and migration of the spindle towards the centre of the egg was the first and most obvious change. This prepares the egg for equal cleavage rather than the usual unequal division which results in the formation of the second polar body. Graham[3] stimulated eggs 12–17 h after ovulation and obtained about 30% "immediate cleavage"[6] in the activated group, whereas Tarkowski[7,8] applied an electric shock to the exposed oviduct 2–4 h after ovulation and obtained activation in approximately 50% but a very low incidence of immediate cleavage. This suggested that the time of activation after ovulation might be important in the type of parthenogenones induced. Eggs were considered to have undergone immediate cleavage only if, at the time of examination, they were morphologically indistinguishable from a normal fertilized two-cell egg—that is, apart from the absence of a second polar body. They resulted from a biochemical or experimental stimulus other than that provided by fertilization. The few eggs with unequal blastomeres were therefore not included in this group.

$(C57Bl \times A_2G)F_1$ females were superovulated and killed at intervals of 2 h, 14–20 h after injection of human chorionic gonadotrophin (HCG). (Ovulation occurs approximately 12 h after this injection.) Oocytes were released from the ampullae into a modified Krebs-Ringer bicarbonate culture medium containing 4 mg ml.$^{-1}$ bovine serum albumin[9] and 100 IU ml.$^{-1}$ hyaluronidase (Koch-Light, ovine testes), and incubated at 37° C in 5% CO_2 in air. After 10 min the eggs were transferred to a hyaluronidase-free medium and culture continued for a further 6 h. Atretic and fragmented eggs were not transferred to the hyaluronidase-free medium as they were ovulated in this state, or resulting from the PMSG-induced ovulation[10].

Eggs were examined under the ×50 magnification of a Wild dissecting microscope to determine the overall frequency and types of parthenogenones induced. These results are presented in Table 1 (groups 1 to 4). Results from a more extensive series in which mice were autopsied 18–20 h after injection of HCG are also presented in Table 1 (group 5). If the results of groups 1 to 5 are combined, 740/757 (97.8%) of the activated eggs had a single pronucleus and second polar body (the first very rarely persists), seven had two pronuclei (0.9%) and ten underwent immediate cleavage (1.3%). Further groups of mice were killed approximately 25 h after HCG and these results are presented in Table 1 (groups 6 and 7). Control eggs were cultured in hyaluronidase-free medium. No spontaneous activation was observed at the time of isolation of the eggs from the oviducts and only in the more aged groups was handling of the eggs sufficient to activate a proportion of the eggs in the control series. In the group 6 (where a fresh epididymal sperm suspension in the modified Krebs-Ringer bicarbonate culture medium described earlier was used as the stimulus) the overall frequency of activation was 73.2% (224/306), but the incidence of the various types of parthenogenones differed considerably from the previous series, with immediate cleavage in 77.7% (174/224). In group 7 (where hyaluronidase medium was used) a similar frequency of activation was obtained (75.4%, 288/382) and a slightly lower incidence of immediate cleavage (62.2%, 179/288).

These results place on a quantitative basis the ageing changes previously observed[5], and probably explain the high incidence of immediate cleavage observed in late insemination by Marston and Chang[11]. This seems to be a more likely explanation than that spindle migration occurred as a direct result of the activation procedure as suggested by Braden and Austin[6], though this central migration might be accelerated by heat[6,12] or other experimental stimuli[7]. A low incidence of eggs with two haploid sets of chromosomes without extrusion of the second polar body was observed in this series. This may be explained by strain variation[13].

In another series of experiments where females were killed approximately 20 h after injection of HCG and eggs were added to a fresh epididymal sperm suspension (group 8), 774/1404 eggs were activated (55.1% overall activation frequency). The frequency of activation was 62.8% (558/888) when similar eggs were added to a sperm-free filtrate (group 9). When aged eggs were added to a sperm suspension (groups 6 and 8), certain factors in the suspension activated the eggs mechanically or biochemically. By filtering the sperm suspension through a 'Millipore' filter (group 9) I concluded that activation is not due to direct (mechanical) stimulation by sperm, but to a factor or factors released by sperm into the culture medium (for example hyaluronidase or other enzymes from the acrosomal region).

My results help to define the conditions needed for the experimental induction of different types of parthenogenones. The critical factor is clearly the age of the oocyte when the stimulus is applied.

Varying the osmolarity of the culture medium also results in different types of parthenogenone[3,4], an effect that may possibly arise through changes resembling those that accompany ageing.

I thank Professor C. R. Austin for his criticism of the manu-

Table 1 Reaction of Eggs 6 h after Addition to Various Experimental Situations

Group	Stimulating medium	Hours after HCG injection when females were killed	Total number of eggs	Activated eggs 1 pronucleus+ 2nd polar body	2 pronuclei	Immediate cleavage	Overall % activation
1.	Hyaluronidase medium	14	172	—	—	—	0.0%
2.	Hyaluronidase medium	16	211	56	1	—	27.0%
3.	Hyaluronidase medium	18	117	89	—	—	76.1%
4.	Hyaluronidase medium	20	137	112	2	1	83.9%
5.	Hyaluronidase medium	18–21	689	483	4	9	72.0%
6.	Fresh sperm suspension	25	306*	50 (combined group)		174	73.2%
7.	Hyaluronidase medium	25	382*	96	13	179	75.4%
8.	Fresh sperm suspension (a)	18–20	1,404	756	34†	18	55.1%
9.	Sperm-free filtrate of (a)	18–20	888	537	9	12	62.8%

* Apparently normal one-cell eggs or immediately cleaved eggs as observed 6 h after addition to the stimulating medium. About 5% of eggs transferred to the hyaluronidase medium (and controls) in the 25 h group were fragmented at 6 h, and these are excluded from the total of group 7 to make the data comparable with those from group 6. No fragmentation was seen at 6 h after activation in the other time groups or in their controls.

† Possibly due to *in vitro* fertilization, so these eggs are not included in calculation of activation frequency.

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Sexual Behaviour and Sexual Motivation in the Female Rat

Is the sexual behaviour of the female rat pure reflex, or does oestrus also stimulate active efforts to approach the male? Male rats will learn to run an alley if rewarded with an oestrous female, and their performance in the alley is then controlled by the same hormone that controls the mating acts, testosterone[1]. Attempts have been made to train female rats to learn an alley in which the reward was a copulating male, but they did not learn to run any faster than others rewarded with an impotent male (and no copulation) (refs. 2 and 3, and M. Williams

and R. F. D., unpublished results). The control females, however, learned very rapidly to run to an impotent male; and it is possible, therefore, that the effects of this (presumably social) reward are so strong as to mask any additional, specifically sexual, reward that mating itself may provide. In the experiment reported here, the choice of an individual female for a potent (copulating) as against an impotent male was examined, using a T-maze.

The animals used were eight young Wistar females, and ten Wistar males preselected for good sexual performance. Under 'Nembutal' anaesthesia 50% of males were castrated and the females ovariectomized. Oestrus was reinstated in the females as required with injections of oestradiol (5 μg given subcutaneously in arachis oil, 48 and 24 h before the test) and progesterone (400 μg given subcutaneously in arachis oil or propylene glycol 8 h before the test). Training took place in a wooden T-maze 25 cm high. The stem measured 27.5 by 30 cm and the two arms were each 27.5 by 39 cm; all three were fitted with opaque sliding doors 15 cm from the end, raised by a string equipped with counter-weights.

At the start of each trial the female rat was placed behind the door in the stem. A potent male was positioned behind the door of one arm, and an impotent male behind the door of the other; which male was in which of the arms for each female was fixed on her first trial by the toss of a coin: thereafter it remained unchanged. To start each trial, the female was released from her compartment in the maze. When she had moved into one of the two arms of the maze (with her whole body excluding the the tail), the male in that arm of the maze was released. The choice and its latency were recorded. The chosen male and the female were left together for a standard interval. This was 2 min during the first trials, but was subsequently reduced to 1 min because mating was reliably obtained in the shorter interval. The duration of access to the potent and the impotent male were thus identical, the only difference being in what they did to the female.

After any trial in which a potent male ejaculated, he was replaced with another from the stock of five; and the impotent male was also changed, so as to equate their novelty. During a

training session trials followed one another without a break. As a rule eight trials were given in each session, though this was not invariable. The sessions were separated by an interval of at least 4 days. The criterion for successful training was eight consecutive turns towards the potent male.

During this part of the experiment the females received an average of 3.5 intromissions during each minute spent with the potent male, and one ejaculation every 2.7 min. The castrated males showed no sexual behaviour other than occasional desultory mounts. All eight females learned to choose the potent male to the criterion, in a mean of 32.2 trials (standard deviation 15.3). Using this criterion, a "criterion risk" (that is the risk of a criterion being reached, given random performance) of 5% is exceeded if more than thirty-one trials are run[4]. To ensure that the criterion had not been reached by chance, the position of the males was reversed for each female as soon as she reached the criterion, and she was then retrained to the same criterion in the same way. All eight animals relearned the task to criterion, in an average of 86.4 trials (s.d. 32.8). The learning curve for this part of the experiment is shown as Fig. 1. This curve illustrates the progressive learning shown by the females. It is clear that attainment of the criterion is the outcome of this gradual learning process, and not a chance effect. It should also be noted that the rats trained in this experiment showed a classic negative transfer, taking twice as long to learn the second as the first response.
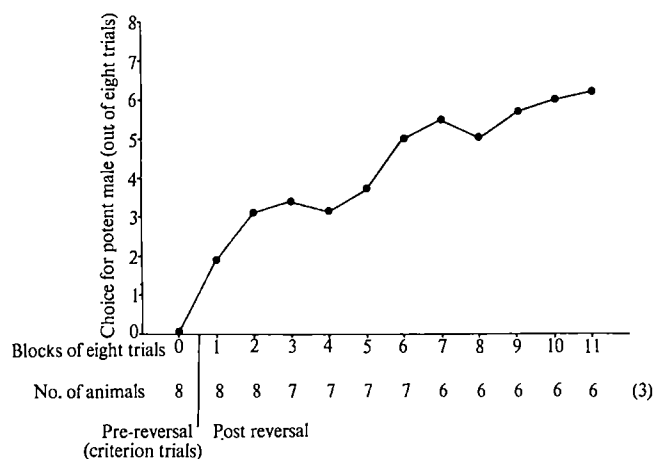
Fig. 1 Choice for a potent, as against an impotent, male by the female rat. This figure shows the course of learning when the position of the males is reversed following original training. The results from an animal are only included in the figure up as far as the end of the eight trials on which criterion was reached. By the eighty-eighth trial most of the animals had reached criterion, and the curve is therefore not continued beyond this trial.

When all the animals had reached criterion, the hormonal determinants of this learned approach to the male were examined. Six of the eight animals were run in the maze in the same way for a further period, in blocks of twelve trials given at weekly intervals. But interspersed among these "oestrous" blocks were blocks of trials similar in every way except that the females were not pretreated with hormones and hence were not sexually receptive. In all 204 "oestrous" trials and 108 "unreceptive" trials were run.

The absence of behavioural oestrus neither reduced the females' preference for the potent males nor increased the latency of the choice. During the 204 trials on which the females were sexually receptive, they chose the potent male on 73%, with an average latency of 4.4 s; on the 108 trials without hormone treatment they chose the potent male on 80% of the trials with an average latency of 2.6 s. On none of the "unreceptive" trials did they show any indications of lordosis. Altogether, then, these findings give no indication that oestrus

involves the stimulation of any behaviour more complex than the unlearned motor patterns characteristically associated with it.

Oestrus is associated with enhanced general activity[5], but seems to be independent of sexual receptivity. Progesterone, which synergizes with oestrogen to enhance sexual receptivity, does not increase such activity[6,7]; and differentiation as a normal male, which virtually eliminates female sexual responsiveness to oestrogens, does not prevent the greatly increased activity that results from ovarian implants[8]. The hyperactivity of oestrus, therefore, does not betoken an effort to seek out a male with which to mate because (1) it can be dissociated from sexual receptivity under several conditions and (2) approach behaviour directed to the male is found to be uninfluenced by ovarian hormones that suffice to produce sexual receptivity, when examined directly.

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Orientation-sensitive After-effects of Dichoptically Presented Colour and Form

McCOLLOUGH[1] discovered that if a grating pattern of (say) red vertical stripes is viewed alternately with one of green horizontal stripes for some minutes, an orientation-specific colour after-effect is observed when viewing a black-and-white test grating. White stripes in a given orientation appear tinted with the hue complementary to the hue presented at that orientation in the original stimulus. McCollough observed that if only one eye was exposed to the original sequence of stimuli, no after-effect was seen when the other eye was used to view the test grating. From this she concluded that the adaptation responsible for the after-effect must occur somewhere in the uniocular pathway before signals from left and right eyes are combined. She suggested as a possible explanation that orientation-sensitive channels in the uniocular nervous system ("edge-detectors") may be colour-coded, so that strong adaptation with bars of red light in one orientation leads to a "minus-red" after-response from the adapted channels to similarly oriented colourless bars. Harris and Gibson[2] have confirmed that the effect persists in conditions ruling out ordinary negative after-images, which Murch and Hirsch[3] have shown sufficient to induce it. Held and Shattuck[4] have demonstrated a corresponding after-effect of colour upon the perceived orientation of test bars.

In view of the reported absence of interocular transfer of this effect[1], the physiological locus of adaptation is of interest

as a clue to that of the presumed orientation-sensitive elements in the human visual system. Following a suggestion by Dr Stuart Butler of Birmingham (personal communication), we have investigated the after-effects of presenting information on colour and orientation separately to the two eyes, and have discovered a curious form of interaction between the two uniocular signals.

The subject sat in a darkened room and viewed with one eye a projection screen (2.15 metres away) on which orthogonal left-oblique and right-oblique black-and-white gratings (luminance 22 cd m⁻² at centre of stripes) were presented alternately for equal periods of the order of 5–10 s, over a total period of 5 min. The patterns subtended 20° × 14° and had a spatial frequency of 2.2 cycles/degree at the observer's eye. (Oblique orientations were used to avoid any bias associated with horizontal and vertical.)

Fig. 1 Two of the test patterns used. The hue of the central patch(es) could be adjusted by the subject to match that of the background.

The subject's other eye was exposed to a uniformly illuminated diffusing screen whose colour changed from red to green as the striped patterns alternated. The visual subtense of the coloured field more than covered that of the striped patterns as viewed by the other eye. The luminances of red and green fields were matched at approximately 34 cd m⁻².

After 5 min of this dichoptic stimulation, subjects viewed a black-and-white test grating (2.2 cycles/degree) surrounded by an orthogonal black-and-white background grating of the same spatial frequency. Various shapes of test grating were used, the commonest being a disk subtending 4.5 degrees at the eye, at the centre of a circular background grating of 27 cd m⁻² subtending 13.5 degrees (Fig. 1a). A later design which proved easier to use employed two oppositely oriented test patches side by side lying in oppositely oriented backgrounds (Fig. 1b). The two test orientations were always used alternately. As well as inviting verbal reports of perceived hue, we used a quantitative null-method of measuring the after-effect. The subject was provided with a (smooth-surfaced) knob by which the test patch could be made slightly red or green to neutralize its perceived hue. The luminance could be independently adjusted to match that of the background. The whole test field (patch plus background) could be rotated to give either orientation of the central test grating. As it turned out that many subjects had an initial bias whereby the test patch appeared greener or pinker than background according to slope even without prior stimulation, the measure adopted for the after-effect was the change in the bias

after adaptation. The bias itself was recorded as the difference between the readings for balance at the two orthogonal test orientations. We also verified that any after-effects of the faint colours imposed on the test patch during the matching process were too small to introduce a significant bias.

A detailed discussion of the results will be published elsewhere, but the most significant findings were as follows: (1) All subjects showed a significant orientation-sensitive colour after-effect of the dichoptic stimulation, most of them spontaneously reporting changes of hue from pink to green or vice-versa as the test grating was rotated through 90°. Subjects differed considerably in the precision with which they could reproduce a match, but in several cases there were significant signs of reversal of the after-effect after a few minutes, particularly in the eye that had received the coloured stimulus. (2) Quite unexpectedly, the initial after-effects in left (L) and right (R) eyes when tested singly were almost always in opposite directions. Table 1 shows a condensed summary of results obtained from nine subjects. As a check, all possible combinations of conditions were used (colours to L/R eye paired with patterns to R/L eye; each orientation paired with Red/Green; test field presented to L/R eye), though not all with every subject.

Table 1 Hues Seen when Viewing Black-and-White Test Grating with either Pattern-stimulated or Colour-stimulated Eye

	Subjects								
	V.M.	B.H.	S.J.	J.M.	E.M.	D.A.	R.M.	C.F.	D.M.
Hues seen with pattern-stimulated eye	S, S S, S	S	S, S S, ?	S, S	S, S	S, S S, ?	S, S S, S	S	S
Hues seen with colour-stimulated eye	C, C C, C	?	C, C C, C	C, ?	C, C	?? ??	C, C C, C	C	C

S: Same as hue originally paired with similarly-oriented grating. C: Complementary to hue originally paired with similarly-oriented grating. ? : Inconclusive result.

After allowing for initial bias, there were no consistent exceptions to the following summary: (a) Seen through the eye that originally received (colourless) patterned stimulation, a black-and-white test grating has the hue originally associated with the same orientation. The measured strength of this effect was found to be variable, and at most roughly half that of the normal McCollough effect. (b) Seen through the eye that originally received coloured but non-patterned stimulation, the test grating has (more weakly) the complementary hue to that originally associated with its orientation.

One possible inference from the results is that some transfer of information between L and R eye channels may be taking place before the stage at which form and colour are associated[5]; but whereas orientational information seems to be transferred correctly, it looks as if colour transfer is antagonistic—that is, as if (say) red light in one eye gives rise to a signal of "minus-red" in the other channel.

An obvious physiological question raised by these results is whether any colour sensitive units at the geniculate or other early stages of the primate visual pathway show signs of complementary sensitivity to colour in the other eye. Inhibitory interaction between pattern-evoked signals from the two eyes has frequently been found in the cat lateral geniculate nucleate [6–8]. Alternatively, is there an efferent pathway whereby the neutral point of the red-green colour signalling system in both uniocular channels is centrally regulated?

We gratefully acknowledge the help of colleagues and

others who acted as subjects, and the financial support of MRC and SRC.

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Diurnal Variations of Water in Developing Secondary Stem Tissues of Eucalypt Trees

Zahner[1] has stated that living cambial tissues must be under moderate to severe water stress almost daily during the growing season because of the great tensile forces which develop in the adjacent mature xylem. We have studied diurnal water variations within the developing tissues of tree stems.

Samples were obtained by removing strips of bark from the stems of *E. regnans* trees and immediately scraping the exposed xylem and phloem surfaces. Each tissue sample was placed in a tared glass tube which was stoppered, weighed and partially immersed in a mixture of dry ice and ethanol. The samples were freeze dried to constant weight, and the amounts of water and dry matter thus obtained. Sampling was done every 4 h during a 24 h period; eight or nine different trees were sampled at each sampling time and mean values were used to plot the graphs in Fig. 1. On the basis of the fresh sample weights, statistical analysis showed that: (1) for xylem, there are significant differences between times as compared with variation between trees within times; the average standard error of a mean is 1.0; (2) for phloem, the mean for 2400 h is significantly lower (1% level) than the mean of values at all other times, which do not differ significantly from each other; and (3) the difference between means for the two types of tissue is highly significant at 0400 h and at 2000 h, and not significant at other times; the average standard error of a difference between two means at a given time of day is 0.63.

On sampling days, meteorological data indicated that sunrise and sunset occurred at about 0510 h and 1900 h respectively. The days were partially cloudy, of high humidity (relative humidity >65%) and of moderate temperature with little wind, so that transpiration would not have been excessive.

During daylight active transpiration begins with a resultant increase of tensile forces, chiefly in the outermost vessels. The operation of these forces withdraws water from the developing tissues, those cells nearest to the vessels being the most affected (for example, ref. 2). The effects of these forces is far-reaching: Wilson *et al.*[3] have shown that the water contents of leaves, stems and roots of herbaceous plants reach a minimum during the afternoon and attain a maximum during the night (see also refs. 4, 5). That is, the water stress would be greater in trees, for the developing stem tissues of the xylem than for those of the phloem. As a result of these conditions, the developing phloem tissues lose water at a slower rate (Fig. 1) than the developing xylary tissues (about 0500 h to 2000 h).

By comparison with the developing phloem tissues, the developing xylem tissues are still subject to a greater water stress at 2000 h. Hence between 2000 h and 2400 h the developing xylary tissues will rapidly withdraw water from the immediately adjacent developing phloem tissues until the water demand of the developing xylem tissues is moderated. Thereafter, all developing tissues will regain water as it becomes available, by way of the mature xylem vessels, from the root system of the tree. These indications support the deductions of Zahner[1] and other workers. The developing phloem tissues will regain their full complement of water at a later time than the developing xylem tissues because of their physical location within the bole of the tree.
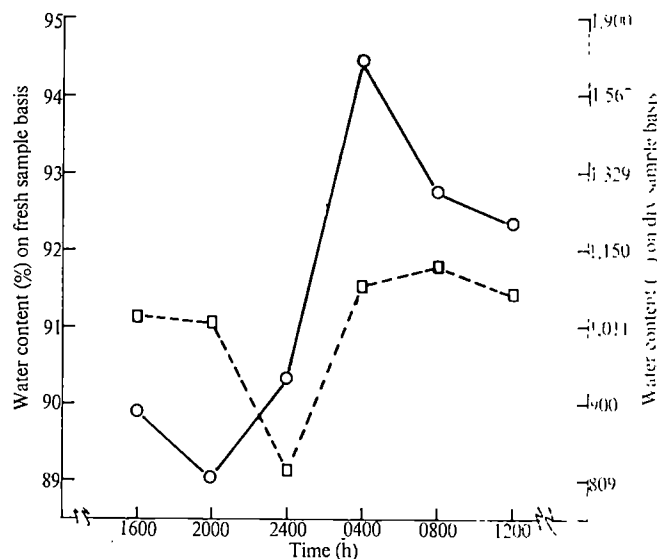
Fig. 1 Water content for developing tissues of *Eucalyptus regnans* tree stems. O———O, Developing xylem tissue; □ – – – □, developing phloem tissue.

If it is assumed that the dry matter, within the developing tissues of a tree stem, remains approximately constant in mass over a period of 24 h, then the samples of xylary tissues taken in the early morning contain about twice as much water as those collected during the late afternoon, early evening period (Fig. 1, right ordinate). These variations in water content imply that diurnal expansion and contraction of the developing cells take place, and may be of considerable physiological significance during the growth of developing secondary cells in a tree stem. Thus, changes in the concentrations of sugars and other soluble substances may be reflected in various interconversions between individual cytoplasmic materials, in the biosynthesis of cell-wall components and in other intra- or intercellular transformations (see also Zahner[1] and Kramer[6]).

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Ancient Scythian Wool from the Crimea

THE origin of fine-woolled sheep has long interested historians and wool biologists. A fine-woolled type was recognized in antiquity, and one of us[1] showed that 2,000 yr old cloth from Palestine, although seemingly made of fine wool to the naked eye, contained a proportion of medium fibres revealed when

to the fifth century BC. It is interesting that it is associated with the Black Sea area, because the legend of the golden fleece, which has been taken to refer to fine wool, is of similar date and is associated with the same area. The only previous Scythian sample examined, from Parzirik in central Asia, was a hairy type with a fleece not unlike that of the sheep in the same area today[5].

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Table 1 Fibre Diameter Measurements (μm)

	System	Diameter range*	Mode	Mean	Distribution	Coeff. of variation (%)	Standard deviation	Percentage medullated	Fleece type
Cloth	(a)	10–25, 29, 31, 35	16	16.5	Skew fine	24.2	4.0	0	Fine
	(b)	9–26	12	14.3	Skew fine	23.0	3.3	0	Fine
Yarn		8–24, 34, 44, 45	13	15.4	Skew fine	38.0	5.9	2	Fine

* Fibres outside the principal range are listed separately.

examined under the microscope. This predominant type at that time formed a generalized fleece in an intermediate evolutionary position between a more primitive hairy type and several modern more highly evolved fleece types, notably the true fine wool, which was already in existence in small numbers at that time[1,2].

The chief feature of this generalized type is a skewed distribution of fibre diameter, in which the bulk of the fibres is fine. It was in existence in the Danish Bronze Age[1] and in ancient Egypt[3]. The true fine wool has a symmetrical diameter distribution, with a mode and mean about 20 μm, and there are suggestions that this went back to the fourth century BC in Palestine[2].

The material comprised two pieces of cloth, one having only one yarn, in the Ashmolean Museum, Oxford, and came from a Scythian tomb (Tumulus I) in the Crimea near the Greek city of Nymphaeum. Its date is fifth century BC.

Whole-mount microscopical preparations were made and diameter measurements carried out on 100 fibres from each yarn using the International Standards Organization method 181 (ref. 4).

The wool fibres had the yellow-brown discoloration common in archaeological specimens with no evidence of the granules associated with natural pigmentation.

Fibre diameter measurements are shown in Table 1. The fleeces are clearly of fine type, although the diameters still have a skewed-to-fine distribution. The means and modes have an exceptionally low magnitude even for fine fleeces. These values are lower than those in the Egyptian wool[3] and were found previously in Danish Bronze Age wool[1] and some Roman samples[2]. The means and modes are comparable with the undercoat of the wild sheep[2]. In spite of the fineness, a few of the fibres had a medulla. This has been noted previously in archaeological specimens, notably in the Egyptian wool[3].

These samples firmly establish the fine wool as going back

Erratum

OWING to an administrative error, Fig. 2 was omitted from the article "Polarization Charging Effect and Thundercloud Electrification" by Zev Levin and W. D. Scott (*Nature*, **240**, 232; 1972).
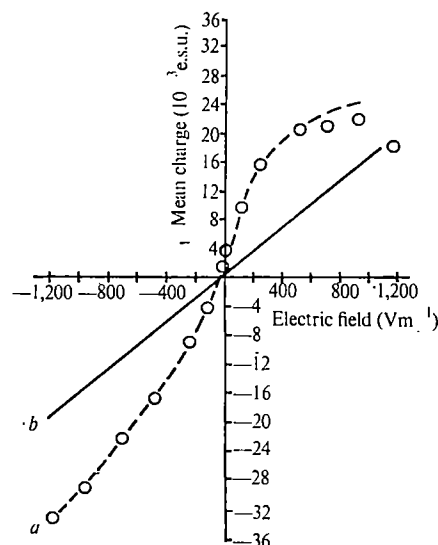
In paragraph 4, line 4 and paragraph 5, line 1 therefore Fig. 1 should read Fig. 2. In paragraph 2, line 5 should include (Fig. 1) after 5,000 V m⁻¹.

BOOK REVIEWS

Linguistic Development

Sentences Children Use. By Paula Menyuk. Pp. xii+165. (MIT: Cambridge, Massachusetts and London, May 1972.) $1.95.

PSYCHOLOGISTS interested in the processes by which children acquire their native language have slowly come to the realization that an analysis of language behaviour in purely descriptive terms is inadequate. Part of Chomsky's revolution in linguistics was to show that grammar is generative—that the speaker's competence consists of rules which allow him to generate grammatically acceptable new combinations of words. If this approach is to be properly applied to child language studies, it will be necessary to analyse children's utterances in more depth and to produce structural descriptions which capture the abstract features which they code. In *Sentences Children Use*, Paula Menyuk states that her purpose is to describe the utterances of children at various developmental stages by "using the techniques of experimental psychology within the framework of a generative model of grammar". The book is devoted to a structural description of the sentences which a group of normal children produced and to a study of their responses in an imitation task. In addition, the utterances and imitations of a small group of linguistically deviant children are analysed.

Menyuk examines the development of both base structure and transformational rules. A case is made that even the early utterances of the child which consist of only single morphemes are nevertheless "sentences" since they are prosodically marked and because they are productively used. She represents these earliest sentences as: topic + intonational marker. Later, multi-morpheme utterances are similarly used generatively; the child does not simply imitate what he hears. This is well known to psycholinguists. What Menyuk adds, however, is a close analysis of the base structure rules. She finds that by the age of three years, all of the children in the normal group have expanded all of the nodes in the base structure, that is, they are able to produce utterances which express all

of the basic categories. This is in contrast to the transformational rules, not all of which are used by all of the normal children surveyed between three and seven years of age.

Another interesting method Menyuk used was to make a careful linguistic analysis of sentences the children produced which deviated from grammatically well-formed ones. Although one may question Menyuk's particular linguistic interpretations, the data are presented for the reader to see for himself, and these observations may prove extremely valuable to students of language who wish to examine the acquisition or development of particular linguistic features.

In spite of the claim to be using the methods of experimental psychology, only one "experiment" is reported: having children imitate both grammatical and deviant sentences actually taken from the production data. In the results, one finds more evidence of what others in the field have claimed—that imitation is not the method of acquisition. Children only imitated structures they were already spontaneously producing and occasionally structures which they were on the verge of acquiring in their productive speech. Furthermore, the length of a sentence was not a factor which determined successful imitation even for children as young as three years and even with sentences up to nine words in length. Structure, not length, determined whether a sentence was successfully imitated.

The same imitation task was administered to a group of children classified as "infantile" in their use of language. Unfortunately we are told very little about this group—how it was obtained, how the children were diagnosed, and how many children were tested. From her results, Menyuk concludes that these children are arrested at an early stage of language development, but one which differs qualitatively from normal-speaking children. She speculates that some kind of short term memory limitation may be responsible for their problems.

One drawback to this book is the inelegant and heavy style of writing. The terminology is unnecessarily convoluted, and explanations often take

too many connecting links for granted. This makes the book difficult to read and easy to misinterpret. The ungrammatical sentences children use nevertheless communicate; the sentences Menyuk uses too often do not. This is a shame, for the book is an important one for showing how a structural analysis can be made. If one can cope with its style, this book offers rewarding insights into the acquisition and development of language structure.

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Joseph Henry

The Papers of Joseph Henry. Edited by Nathan Reingold. Assisted by Stuart Peirson, Arthur Molella, James Hobbins and John Kerwood. Vol. 1: December 1797–October 1832. Pp. xxxix+496. (Smithsonian Institution: Washington, December 1972.) $15.

To those historians who look for major contributions to modern science, nineteenth-century America cannot but seem an arid region. Americans made very few discoveries of important phenomena, or wide generalizations which brought into relationship facts which had previously seemed isolated. Exceptions to this generalization would include Joseph Henry who, independently of Faraday, discovered electromagnetic induction; and Willard Gibbs who introduced thermodynamics into chemistry. But as Americans themselves came to recognize, by the end of the nineteenth century America had become a dominant power in technology without yet emerging as a great centre of pure science. One might expect then that while filial piety might move those at the Smithsonian Institution to publish Henry's papers, the resulting volume would be of small interest to any but specialists. This would be quite wrong: for Nathan Reingold and his associates have produced a work which should be of great interest to all those concerned with science and its development. They have shown once again that there is no need for parish-pump history to involve Chauvinism or antiquarianism; but that on the contrary the close study of a scientist against his background can

illuminate the way science works, in ways that the enumeration of major contributions to modern science cannot.

The volume, the first of many, presents us with what the editors describe as "a broad documentary history of a period and a place, not merely a narrow recital of events in a career". They have drawn upon letters, diaries, lecture-notes, and minute-books; most but not all of which have immediate reference to Henry. Their aim is to show the growth of an American scientific community; an entity which was frequently appealed to by philosophers in nine-teenth-century America, but which at the beginning of the century would have been hard to define. Benjamin Franklin had not founded a school, and the two leading scientists of the period of the Revolution, Count Rumford and William Charles Wells, had both gone to Europe. In succeeding volumes we shall no doubt see men of science coming to regard themselves as a community having common interests and purposes; but in this first volume, which ends with Henry, at the age of thirty-four, about to take up a Chair at Prince-ton, the nature of science and its rela-tion with technology is the chief point at issue.

Here we find that though Henry, in an introductory lecture on chemistry printed here, speaks of the need for "speculative science", he and his con-temporaries do not seem to have dis-tinguished pure and applied science. The distinction Henry makes is between practice guided by genuine knowledge, and the mere empiricism of inventors. We find Henry himself advising indus-trialists on the magnetic separation of iron ore, and deploring patent laws which seemed to him to force scientists to make a choice between making their discoveries freely known, on the one hand, and profitable on the other. The emphasis on the applications of science which we find in these writings of Henry's is very like that in the lectures of his older contemporary, Humphry Davy, and does not in itself represent anything distinctively American. In the same way, "science" in America in the early years of the nineteenth century seems to have meant particularly natural history, geology, meteorology, and terrestrial magnetism; and it was from this last study that Henry moved on to electromagnetism. Mathematics were indeed cultivated, but it seems to have been the "mixed" or applied branch rather than higher mathematics. Very much the same situation prevailed in Britain, where critics of the *status quo* called for more support for mathematics from a government which was not un-generous in its support of descriptive sciences; urging that applied mathe-matics could be the most useful of sciences.

Not only was the question of utility differently handled in Henry's day from the way it is in ours, but the boundaries between the various sciences were differ-ently drawn. Thus when Henry made what were then the most powerful electromagnets in the world, the pro-fessors who urgently wrote asking for one to demonstrate before their classes wanted it for their chemistry lectures; and not, as we might expect, for the mathematics or natural philosophy classes. This again was not an Ameri-can classification of sciences; Volta's discovery had shifted electricity into chemistry, and Faraday held office only in the chemical section of the British Association. There were distinctive features about the way science was car-ried on in America, but the great general questions seem to have been similarly handled on both sides of the Atlantic.

Henry's work on electromagnetism was done when he was professor of Mathematics and Natural Philosophy at the Albany Academy; and the docu-ments tell us much about the function-ing of this body. Again, it does not fit modern classifications, being neither a high school nor a college; it had some free places, one of which Henry got, and it prepared some students for college and others for a career. Henry, like Faraday, thus became a Professor with-out ever getting a first degree. Mathe-matics were regarded by the governing body of the Academy as perhaps the most important branch of knowledge taught there; and we find discussions of which textbooks should be prescribed, and what philosophical instruments were necessary. Albany also had an Institute, on the Napoleonic model, one "class" of which was devoted to science; in which Henry became a leading light. We find here the letters and minutes relating to Henry's appointments to Albany and Princeton, which have a certain fascination.

Henry's predecessor at Albany was sacked for being involved with a female of low character; Henry seems to have been immune from such temptations, to judge from what we find here of his life. We see his student notebooks, and a field-trip diary; his curiously formal letters to his cousin Harriet who became his wife, including some making up a row; other family letters; and letters illustrating his activities as a land-sur-veyor and then as a Professor. Even on his honeymoon he spent some time investigating scientific apparatus at Yale; earlier he had visited West Point Military Academy which, in the tradi-tion of the Ecole Polytechnique, seems to have provided the best scientific training available at that time in America. In minutes and correspond-ence about the *Transactions* of the Albany Institute and Silliman's. *Ameri-*

can Journal of Science, we learn much about the dissemination of science at this time; and see Henry and Silliman working out demonstration experiments in their correspondence. We also see Henry being prickly about his priority, and about the amount of credit due to his co-worker, Philip Ten Eyck.

We must then congratulate the editors on their selection, and the publishers on producing the book hand-somely at what is by today's standards a low price; and look forward to the volumes to come. The notes and index will provide a valuable "who's who" for students of American science; and we see Joseph Henry the man against a rich background.   DAVID KNIGHT

About the Ultrapure

Ultrapurity: Methods and Techniques. Edited by Morris Zief and Robert Speights. Pp. xv+699. (Marcell Dekker: New York, June 1972.) $37.50.

EDITORS who attempt to cover ultra-purity in a single book, even a big book, must of necessity be bold and the magnitude of the task can be gauged from the appendix (fifty-three pages) entitled "Information Sources for Ultrapurification and Characteriza-tion" which, although it gives incom-plete coverage, lists fifty-two informa-tion centres and twenty-three journals concerned with purification.

Zief and Speights in a short preface to the twenty-two chapters provided by twenty-four authors claim that the book brings together for the first time the preparation, handling, containment and analysis of ultrapure materials. There is no general introduction nor summary so that neither the philosophy underlying ultrapurification nor the condition necessary for the establish-ment of purity is discussed.

The book opens with a discussion on the preparation of samples of alkali halides suitable for use as optical com-ponents, scintillation counters and solvents and the next chapter deals with the production by frontal-analysis chromatography of specimens of organic solvents for ultraviolet spectro-scopy. As the author of the chapter on pure sodium and potassium is employed by Atomics International presumably the samples of these metals are intended for use in the atomic energy field. The sublimation of phosphorus pentoxide is described for the production of low-cost specimens which can be resublimed without the formation of a residue and can be used for the preparation of ultrapure ortho-phosphoric acid. The chapter on the purification of proteins by membrane ultrafiltration depicts equipment for the removal of salts and of certain proteins

provided they differ sufficiently in properties. Short chapters on the purification of *p*-xylene by partial freezing and on the purification of isopropylbenzene by preparative gas–liquid chromatography record the processing of relatively small samples. The discussion on fractional distillation (nineteen pages) emphasizes the steps which must be taken to protect the samples against contamination by the atmosphere. The author of the account of dry-column chromatography expresses the hope that workers will begin to use this technique. The importance of the nature of the impurities in the starting material for the preparation of pure water is emphasized and the production of specimens of low electrical conductivity and for use in the electronics industry are considered. The difficulties in the preparation of pyrogen-free and particle-free water are mentioned and the chapter closes with the statement, "Ultrapure macroscopic water can be considered to contain microparticles based on the isotopes of hydrogen and oxygen". However, changes in isotopic composition of water during purification are not discussed and the preparation of samples of precise density is, therefore, not reported. There is a straightforward account of the purification and analysis of cholesterol.

The section on "Handling" and "Containment" would have been better written under a single heading because the chapter "Contamination Problems in Trace-Element Analysis and Ultrapurification" presents useful information on storage vessels which is covered again in a slightly different form in the chapters "Glass Containers for Ultrapure Solutions" and "Vitreous Silica". A reader of "Airborne Contamination" would have to look elsewhere for details but is provided with only nine references for this purpose. The chapter entitled "Ceramics" discusses eighteen ceramics in nine pages.

The twenty-four page chapter on "High-Purity Chemicals—A Challenge to Practical Analysis" summarizes briefly the determination of major and minor constituents and is written from much first hand experience. The titles of chapters on "Emission Spectroscopy", "Flame Spectrophotometric Trace Analysis", "Neutron-Activation Analysis", "Visible Spectrophotometry" and "Coulometric Titration" sufficiently indicate their contents.

Much tabulated data is given but the quality of presentation is very uneven; some chapters are difficult to read and are incomprehensible in places due to errors—for example, "A good syringe pump, set at the optimum flow rate, is invaluable for ironing and partial clogging and airflow inconsistencies".

The book jacket states that "This work is directed to all those working in research, development, or analysis of ultrapure products—electronic engineers, analytical chemists, clinical chemists, geochemists, oceanographers, material scientists, and environmental researchers". In my opinion this volume of loosely coordinated chapters attempts too much and as a result many workers in the above mentioned fields may decide to follow the advice given to analysts on page 527, "Specialized applications to specific problems must be sought in sources best known to the individual analyst". Unfortunately most applications of ultrapurity are specialized. E. F. G. HERINGTON

Air Pollution

Air Pollution. By W. L. Faith and A. A. Atkisson. Second Edition. Pp. viii + 393. (Wiley: New York and London, December 1972.) £8.65.

WHEN I edited a book with the same title in 1957, public enemy number one, from the point of view of air pollution, was the coal fire, and number two grit and coarse dust, for example, from chain grate stokers. This book illustrates the fact that, in Europe as well as in the USA, public enemy number one is now the internal combustion engine, and number two is SO_2. The oxides of nitrogen can undergo a photochemical reaction with unburnt hydrocarbons in conditions of intense sunlight and long standing inversions, and so the car is blamed for the Los Angeles smog and a whole chapter is devoted to photochemical air pollution. The CO and unburnt and partially burnt hydrocarbons given off by the car are a consequence of bad combustion and so high fuel consumption, whereas, on the contrary, oxides of nitrogen are primarily a consequence of high combustion temperatures and excess combustion air, while lead is emitted because its addition to the fuel provides a cheap way of operating high power compact engines on a large fraction of the total petroleum.

This second edition is changed from the first edition of 1959 in several ways. First, there is an increase in the emphasis on tall stacks, the use of which reduces the local maximum ground level concentration by spreading it further away, but is not a final solution to the problem when there are enough stacks in a region to combine their long distance effects. The main formulae for dispersion were available 15 years ago, but more work is recorded on effects of tall buildings, irregular terrains, inversions, "fumigation" and multiple stacks. Second, an account of the development of air quality standards and emission regulations in the USA is

added. Then automobile exhaust in the earlier edition has been extended to cover vehicle testing on chassis dynamometer, pollution control methods, two pages only on diesel exhausts and two on aircraft emissions.

The chapter on "Social Origins of Air Pollution" takes what one can call a five-year forward legal-economic look, but completely fails to take account of what the rest of the world can see, that there is no real solution to the pollution and other problems as long as the USA continues to base its economy on a fuel and other resource consumption which is six times the world average. Pollution Control, treated as a problem in isolation from others, can only lead to such results as the US proposed standards for car exhaust emission, causing the manufacturers to fit afterburners and exhaust gas recyclers which cause an increase in the fuel consumption and the engine size and the effective use of which cannot be ensured for long after the car is used. M. W. THRING

Degree of Belief

Probability, Induction and Statistics: The Art of Guessing. By Bruno de Finetti. Pp. xxiv + 266. (Wiley: New York and London, November 1972.) £6.50.

DE FINETTI is perhaps the most brilliant worker in the field of probability this century. His work is little known in Britain because he writes mainly in rather difficult Italian, and because he does not publish in statistical journals, where the main operational material on probability has appeared. Here we have the opportunity to read, in English, about some of his ideas. No one interested in probability should fail to read this book.

His view of probability is that it is always "a measure of the degree of belief of a given subject in the occurrence of an event (proposition)". The book is not written as a unit, but consists of eleven papers divided into three main groups. The first group consists of papers on the operational foundations. His philosophical attitude is essentially behaviouristic, and probability is measured and understood by the subject's attitude to decision problems. In these papers he discusses, amongst other things, how this measurement might be performed. Statisticians who keep saying the prior distribution is unknown should read this section. The next group of papers is concerned with the axiomatic foundations of probability: in particular, whether it is finitely or σ-additive. This section is really only suitable for the reader equipped with the necessary technical knowledge of measure theory. Frankly it leaves me

unimpressed, for it seems to depart from the operational standards of the rest of the book. How, for example, can you choose an integer at random? Such a choice is at the root of the axiomatic difficulties.

The third section is devoted to induction and statistics, not in a narrow, technical sense but in the widest meanings of these terms. Adherents of the subjectivistic view of probability have been slow (and perhaps a little surprised?) to appreciate the catastrophic effect their ideas have on the practical problems of science. All scientists who are interested in the methodology of science could read parts of this section with profit.

The translation has not been well done and de Finetti's meaning is not always transparent. But this is an important book and should not be passed over on that account.

D. V. LINDLEY

Freudian Controversy

Fact and Fantasy in Freudian Theory.
By Paul Kline. Pp. x+406. (Methuen: London, January 1972.) £5.

THE controversy about the place of Freud's thoughts in general psychology shows no sign of abating. It is largely maintained not by psychoanalysts, who unfortunately and in contrast to Freud show now all too little interest in general psychology, but by efforts at refutation and more or less bad tempered attacks from academic psychologists. In this situation Paul Kline's book is particularly welcome because it breaks away from this traditional pattern. Kline is an academic psychologist with high standards of scholarship, competence in research methodology and fully conversant with Freud's work—in itself a rare combination. Each chapter of his book is devoted to a study of the "objective scientific evidence" relevant to one of the basic postulates in psychoanalytic theory. Kline begins with a concise definition of the postulate, citing chapter and verse from Freud which enhances the book's value as a reference work; he then discusses the general methodological problems of research in that area and presents in schematic detail the empirical work with his own critique of its methodological adequacy. While Kline cites well over 600 references, he acknowledges that this is not comprehensive, and it would be churlish to cite omissions. He finds experimental support for some major Freudian concepts, such as repression, and certain personality constellations even though their aetiology in childhood remains unconfirmed.

Many experimenters have demonstrated remarkable ingenuity in devising testable hypotheses from psychoanalytic theory and designing situations in which they could be investigated. There is, for example, the well known work of Hall who submitted the manifest dream content of men and women to statistical analysis which lent strong support to the idea of an Oedipal complex and castration anxiety even though he had of course no access to what Freud regarded as essential, namely the latent dream content. This work certainly refutes the notion that dreams are the result of randomly firing nerve cells. The situation is less satisfactory with regard to another central part of the theory—some defence mechanisms. Kline rightly emphasizes that the methodological difficulties here are nearly insurmountable. Take, for example, projection, a concept for which there is a very large amount of clinical evidence and which has such widespread face validity that it has become accepted outside the technical jargon of the theory. Notwithstanding some efforts the experimental evidence for the mechanism is just not good enough. The crux of the difficulty is of course the experimental approach to the concept of the unconscious. The thief who cries "Stop, thief" is projecting as a deliberate purposeful disguise but not in the sense of the Freudian defence mechanism which requires that the motivation for projection be inaccessible to consciousness. One can take it from Kline that this discrimination is beyond the power of current research methods. Whether the unconscious should therefore be eliminated from psychology as a science, much as the one-time useful fiction of phlogiston was dropped, or whether it should, as Foucault seems to suggest, be regarded as the necessary identification of a border-line beyond which science cannot proceed, or whether clinical evidence should finally achieve scientific status within a framework of research which is concerned with meaning rather than mechanisms, is a question that Kline does not raise. In his careful and cautious fashion he lets the matter rest with stating that projection has not been experimentally established.

Where Freudian propositions are experimentally supported, Kline, in an effort at reconciliation with academic psychology, examines relevant predictions from theories of learning and concludes "that in most cases the Freudian phenomena could be fitted into a model derived from theories of learning but that these theories on their own could not have predicted the clinical observations. . . . So, far from regarding learning theory models and psychoanalytic theory as opposed, we consider them to be closely related—the Freudian theory supplying the details of the learning procedures". Much as one would like a rapprochement, this suggestion may throw out the baby with the bathwater.

Notwithstanding the excellence of Kline's search for evidence, the value of many of his careful and critical comments and the usefulness of his book for reference purposes, one is left with a feeling that some of the major challenges which psychoanalysis presents to academic psychology have been avoided rather than elucidated.

MARIE JAHODA

Solar System Guide

The Solar System. By Z. Kopal. Pp. 152+14 plates. (Oxford University: Oxford, London and New York, January 1973.) £2.25 cloth; £1 paper.

OUR knowledge of the solar system has advanced by leaps and bounds during the last decade. For example, twelve men have walked on the surface of the Moon and spacecraft have photographed in detail the craters, volcanoes, mountains and valleys of Mars. In the next decade many more ambitious projects are planned. Spacecraft will start out on their journeys to Jupiter and Saturn, others will be soft landing on Mars to search the surface for traces of life. By 1975 the Skylab should be set up and man will at last be able to cast off the atmospheric cloak that continuously hampers ground based observations.

All these past achievements have been fully covered by the news media and in consequence a great deal of interest and enthusiasm has been engendered among the nonscientific members of the public. Now in all new fields a guide is needed if we are to get the maximum benefit from our travels. This is exactly what this book sets out to be—a guide to the solar system. In the introduction it states that its aim is to summarize for the nontechnical reader the principal features of our present knowledge of the astronomy, physics and chemistry of the solar system.

It succeeds admirably. Zdeněk Kopal must be congratulated on writing an excellent book, a book which was a joy to read and which takes us on a fascinating tour of our neighbouring planets. It breaks away from the old fashioned approach of treating every planet as a separate entity and instead stresses the important similarities and differences between the members of the solar system. Comparisons are even made between our solar system and the possible planetary companions of nearby stars. It is also up to date, containing details of the latest Apollo, Mariner and Venera results.

I would like to congratulate Professor Kopal on a job well done and to wish his book the great success that it deserves.

DAVID W. HUGHES

CORRESPONDENCE

Citation and Distinction

SIR,—I previously indicated[1] that frequency analyses of the *Science Citation Index* could help forecast Nobel Prize winners. A number of people have pooh-poohed this simple technique. Consequently, it is of interest to note that all of this year's Nobel Prize winners again were among the list of most frequently cited authors. Two of them were anticipated in my article, in which I gave a list of the fifty most cited authors for 1967, using the 1967 *SCI* as the data base. We have, since then, used the annual *SCI*s from the years 1961 through 1971 (except 1962 and 1963 which were not available then) to compile a list of most frequently cited authors. Out of more than 1.8 million authors cited, only 42,000 were cited at least thirty times in a single year during this nine-year period. However, less than 2,100 were cited more than 1,000 times. In this list will be found all of the Nobel Prize winners for 1972 and also winners for the preceding five-year period with few exceptions. Thus, the Nobel Prize winners were members of an elite group consisting of the top 0.1 per cent of all cited authors.

If any of your readers can propose another algorithmic procedure for measuring scientific impact, let him come forward. In the meantime, if scientific journalists, among others, wish to know where the action was, is, and will be, they would do well to look into this method. We recently used a similar technique to determine the relative "impact" of journals[2]. In spite of the snide remarks of those[3] who prefer the world of subjectivity, the latter study has caused a considerable amount of soul searching amongst those seeking a rationale for thousands of infrequently cited journals.

Yours faithfully,
EUGENE GARFIELD

Institute for Scientific Information,
325 *Chestnut Street,*
Philadelphia, Pennsylvania 19106

[1] Garfield, E., *Nature*, **227**, 669 (1970).
[2] Garfield, E., *Science*, **178**, 471 (1972).
[3] Anonymous, *New Scientist*, **56**, 464 (1972).

Reprint Distribution

SIR,—The letter from Dr L. G. Johnson[1] prompts me to take up the problem of reprint requests from the point of view of the author.

I recently described a modification[2] of a widely used method[3] for measuring protein concentration. After the title had appeared in *Current Contents* the initial trickle of reprint requests swelled to a torrent and passed the 2,500 mark before subsiding to the present one or two per day. In my paper I attempted to balance the advantages of my method against its procedural disadvantages. Yet how many requesters, before writing, saw my paper and assessed whether the new method might on balance be useful? At most about 15 per cent since this group copied my mailing address from the paper. The remaining requests carried (to the despair of the Cambridge Post Office) the address given in *Current Contents*.

Since I could not supply everybody I gave the 15 per cent first priority. This is rough justice since my paper was presumably accessible to this group. On the other hand, it was no doubt inaccessible to many among the 85 per cent. Here I have in mind workers in undeveloped and scientifically underprivileged countries. These became my second priority.

Dr Johnson refers to possible mistaken impressions about working conditions of American scientists. In my view the prevailing impression is not that they are cushioned, by computer-based retrieval systems, so escaping the day-by-day work of reading through the literature, but rather that too many Americans (and too many non-Americans) restrict their reading to published contents lists and to the reprint request system even when, in many cases, adequate libraries and copying facilities are close at hand.

Because of his isolation Dr Johnson asks not to be numbered among the abusers of the reprint system. However, the extent of his isolation may not be widely recognized. I would suggest that his form of request include the information that the alternative to receipt of a reprint is a slog through hundreds of miles of Injun territory. The ubiquity of the Hollywood western would ensure a favourable reply to every request.

Yours faithfully,
E. F. HARTREE

ARC Unit of Reproductive Physiology and Biochemistry,
307 *Huntingdon Road,*
Cambridge CB3 0JQ

[1] Johnson, L. G., *Nature*, **242**, 143 (1973).
[2] Hartree, E. F., *Analyt. Biochem.*, **48**, 422 (1972).
[3] Lowry, O. H., Rosebrough, N. J., Farr, A. L., and Randall, R. J., *J. Biol. Chem.*, **193**, 265 (1951).

Grafting Neologisms

SIR,—Biomedical vocabulary, specialized for centuries, expands with our knowledge. *Symbiosis* ("living together") connotes an intimate physical and physiological relationship between two organisms. *Prosthesis* ("placing onto") describes attachment of devices to increase comfort, health, or convenience: false teeth, artificial limbs, and so on.

Recently, machines that sustain essential life functions have been developed. Kidney machines clean blood of wastes when natural kidneys fail; heart-lung machines oxygenate and circulate blood during heart surgery. Soon a new type of device, artificial hearts, will be available. (These devices have already been tested successfully in calf, dog and baboon).

A seminar here has considered issues of technological assessment and moral evaluation of such devices as an artificial heart. We noted a lack of clear terms to describe relationships involving such technologies. "Man–machine symbiosis" is inadequate, since it implies two living partners. Machines are not properly candidates for symbiosis; they fulfil physiological needs but are not themselves living. They exist solely for service to their organism-associates, which in turn depend upon them for life, and not simply for comfort or convenience.

I submit to you and your readers two neologisms, hopefully useful for discussion of these organism-mechanism relationships—relationships promising increasing importance in future centuries of biotechnics.

Firstly, *epallobiosis* (ĕp-ăl′lō-bĭ-ō′sĭs ; *epallobiotic*, adj.) refers to the dependency of an organism on an external life-support system, e.g., the already well known heart-lung and kidney machines.

Secondly, *enthetobiosis* (ĕn-thĕt′ō-bĭ-ō′sĭs ; *enthetobiotic*, adj.) captures the relationship of "life dependent upon intoplacing" of a mechanical device (implant). The prefix *ep-*, emphasizing dependency, would here overburden pronunciation ; context will suffice to imply relationship that is not casual but critical.

Yours faithfully,
ROBERT ROGER LEBEL

The Jesuit School of Theology at Berkeley,
1735 *Le Roy Avenue, Berkeley,*
California 94709

Announcements

Erratum

IN the article "Radio Sources identified with Optical Objects using Precise Radio and Optical Positions" by H. Gent *et al.* (*Nature*, **241**, 261; 1973), line 10, paragraph 6, should read "The counts quoted in ref. 1 show that the probability of finding a stellar object of neutral colour brighter than 20 mag in the combined error regions for the 11 sources is only 1 in 50".

Corrigendum

IN the article "Cigarette Smoke: Effect of Aqueous and Nonaqueous Fractions on Mitochondrial Function" by C. Gairola and M. I. H. Aleem (*Nature*, **241**, 287; 1973), the cigarettes referred to are the 1R1 University of Kentucky Research Cigarettes and not IRI research cigarettes.

International Meetings

April 30–May 2, Instrumentation in Vacuum Processes. (Meetings Officer, The Institute of Physics, 47 Belgrave Square, London SW1.)

May 1–2, Molecular Weights of Industrial Polymers. (Dr R. Dietz, Division of Chemical Standards, National Physical Laboratory, Teddington, Middlesex.)

May 2–6, Protides of the Biological Fluids. (Simon Stevin Instituut, Jerusalemstraat 34, B-8000 Brugge, Belgium.)

May 3, The Role of Sulphur Dioxide in Food Processing. (Society for Chemical Industry, 14 Belgrave Square, London SW1.)

May 3–4, Minicomputer Interfacing. (Lisa Spaducci, Polytechnic of Central London, 115 New Cavendish Street, London W1.)

May 4, Applied Functional Analysis in Teaching and Research. (Secretary, The Institute of Mathematics and Its Applications, Maitland House, Warrior Square, Southend-on-Sea.)

May 5–12, Food Group Annual Tour. (Mr P. O. Dennis, Brooke Bond Oxo Limited, Witneys Technical Centre, Trojan Way, Purley Way, Croydon, Surrey.)

May 7–9, Tenth Annual Rocky Mountain Bioengineering Symposium. (N. B. Kinding, Dept of Electrical Engineering, University of Colorado, Boulder, Colorado 80302.)

May 8, International Symposium on Crop Protection. (Secretary, Faculteit van de Landbouwwetenschappen, Coupure Links 533, B-9000 Gent, Belgium.)

May 8, The Application of Agricultural Science and Technology to Development. (Assistant Secretary, Society of Chemical Industry, 14 Belgrave Square, London SW1.)

May 8–9, Fluvial Processes and Sedimentation. (Dept. of Extension, The University of Alberta, Edmonton, Alberta.)

May 9, Chemical Engineering Contribution to Medicine and Health Care. (Mr R. Mason, Institution of Chemical Engineers, 16 Belgrave Square, London SW1.)

May 13–18, The International Congress on Noise as a Public Health Problem. (Office of Noise Abatement and Control, US Environmental Protection Agency, Washington DC 20460.)

May 14–18, Second Australian Symposium on Analytical Chemistry. (Mr L. S. Dale, Australian Atomic Energy Commission, Research Establishment, Private Mail Bag P.O. Sutherland, NSW 2232, Australia.)

May 14–17, Fifth International Course on Transplantation. (Dr R. Triau, 17 Boulevard des Belges, Lyon 69003, France.)

May 14–21, The Use of Artificial Satellites for Geodesy and Geodynamics. (Professor George Veis, National Technical University, Athens 147, Greece.)

May 15, Radiationless Transitions in Aromatic Molecules. (Dr O. L. J. Gijzeman, The Royal Institution, 21 Albemarle Street, London W1.)

May 17, Mathematics in Marketing. (Secretary, The Institute of Mathematics and Its Applications, Maitland House, Warrior Square, Southend-on-Sea.)

May 17–19, The Future of Scientific and Technical Journals. (Program Chairman, John Phillips, Bldg. 2–8 RCA, Camden, New Jersey.)

May 18, Specific Cell Adhesion. (Dr R. C. Hughes, National Institute for Medical Research, Mill Hill, London.)

May 23, Cancer Care—Assessment of the Present Position. (Mr P. A. Sturgess, Assistant Secretary, Marie Curie Memorial Foundation, 124 Sloane Street, London SW1.)

May 24, Anaesthesia in Laboratory Animals. (Secretary, Dr R. J. Ward, Carworth Europe, Huntingdon Research Centre, Huntingdon.)

May 25–26, New Developments in Diagnosis and Treatment. (Allegheny General Hospital, 320 East North Avenue, Pittsburgh, Pa. 15212.)

May 28–30, Second Scientific Congress at Istanbul. (Professor Dr E. T. Cetin, General Secretary, Medical Faculty, Dept. of Microbiology, Tropical Diseases and Parasitology, The University, Istanbul.)

May 30–June 1, The Use of Low Energy Accelerators. (The Meetings Officer, The Institute of Physics, 47 Belgrave Square, London SW1.)

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The Cost of Asking for the Moon

THE United States Environmental Protection Agency has only itself to blame for the situation in which Mr William D. Ruckelshaus, the administrator, has had to climb down about the 1975 regulations proposed for automobile exhaust emission (see page 491). Nobody will quarrel with the general aim of the regulations, promulgated under the terms of the Clean Air Act of 1972, that city air should be cleaner and that automobiles should dirty it less than they do at present. But the 1975 regulations were unrealistically stringent, the methods by which they were to be achieved were hardly the most suitable and even now there must remain serious doubt as to whether the mere postponement of the enforcement of the Clean Air Act on automobiles is wise, let alone practicable.

In these days when even students in elementary schools are being urged to take to heart the principle that a system is a system is a system, it is absurd that the United States Administration and Congress between them should have embarked on the laudable cause of reducing the amount of pollution in the streets of city centres by imposing particular restrictions on the percentages of various pollutants to be permitted in the exhaust of all motor vehicles, wherever they happen to travel. The trouble is, of course, that there can be no assurance that the restrictions originally intended for 1975 will bring about the improvement of air quality desired. In the last resort, what matters is the question of how damaging are the concentrations of carbon monoxide, sulphur dioxide and nitrogen oxide expected to be on the health and welfare of people, and this is a topic on which more research is needed. To tell from what Mr Ruckelshaus said this week, there is a long way to go before the effects of nitrogen oxides will be defined with any accuracy, but it is already clear that the first gloomy forecasts, on which the original exhaust standards for 1976 were based, were too pessimistic; it looks as if this part of the exercise will be relaxed. But, then, there is no certainty that the air quality in city centres, those of Los Angeles and Chicago in particular, is linearly related to the numbers of motor cars found there at any time—other sources of pollution are relevant. It is, however, certain that imposing restrictions on the emission of pollutants from cars that travel the wilds of Montana and Wyoming is for the most part entirely irrelevant to the concentration of carbon monoxide and sulphur dioxide, not to mention hydrocarbons, in city centres. One of the fundamental weaknesses of Mr Ruckelshaus's now abortive attempt to clean up the pollution of city centres is that it has been too much concerned with the performance of individual machines and not with an analysis of the whole system by means of which city traffic contributes to city pollution.

The second fundamental aspect of the case which Mr Ruckelshaus has now abandoned is that the new standards were to be applied according to a timetable which is certainly arbitrary and possibly unrealistic as well. It is entirely laudable to seek to clean up the streets of city centres, but it must surely be the case that the cost of doing so must increase disproportionately with the foreshortening of the time scale. At this point, the automobile manufacturers have had just under two years in which to provide means of removing all but ten per cent of the pollutants in the standard motor car roughly eighteen months from now. Whatever complaints may now be levelled against the automobile manufacturers in Detroit, there can be very little doubt that a period of less than four years is ludicrously short for the provision of what is essentially a radically new kind of automobile engine, with quite different characteristics from those put on the market in the recent past. In the circumstances, it is no wonder that nobody at this stage can put his hand on his heart and say that the catalytic converters in which Detroit has been working will perform satisfactorily and last for the statutory 50,000 miles. And although there has recently been great scorn for the slowness of American manufacturers to follow the Japanese both with the development of rotary engines (to everybody's surprise, now capable of being cleaner than conventional internal combustion engines) and with the development of engines fed at different points with gasoline mixtures of different strength, it tends to be forgotten that Japanese manufacturers have had a head start through their early acquisition of patent rights and that, in any case, these new devices have not yet been applied to vehicles as big as those now used in the United States.

What else might the Administration have done? Of the need that all suppliers of vehicles in the United States should meet the same standards, there is no doubt. At least so long as the cost of making engines which are clean is likely to be greater than the normal, it is unreasonable to expect that manufacturers will off their own bats adopt progressively more stringent standards. If air pollution in city centres is a substantial problem, it is entirely proper that governments should seek to control it by specifying the regulations which it considers must be met. It is not, however, an unpedantic question to ask whether responsibility for satisfying whatever criteria are laid down should rest not with the manufacturers of motor cars but with those who use them. If it were possible to show that air pollution in cities is linearly related to the car population there, it might still be more equitable to require merely that those who choose to drive cars in city centres are responsible for making sure that their vehicles are fitted with catalytic converters or otherwise respond to specified criteria. Individuals would then be able to choose, from a knowledge of their own habits, whether they should buy a clean car or a standard car, recognizing that in the second case they would have to refrain from driving about city streets. It is true that many Americans would regard such a discrimination between vehicles as an assault on the inalienable right of all Americans to drive where they will. But is it not absurd to impose a uniform restriction on everybody simply so as to preserve the illusion that everybody is free?

The truth is that the preservation of air quality in city

centres must in the long run be determined by a judicious combination of specifying criteria which individual vehicles must satisfy when they happen to be in city centres and the restriction of the numbers of vehicles which are able to get there. There is at least a case for thinking that the benefits that might be derived from the hastily devised catalytic converters, dubious in their efficacy as they are, could at least in part have been achieved simply by saddling each city centre motor car with a tax or levy equal to the cost of the extra equipment. Sooner or later, those who use motor cars will be forced to temper their belief in the freedom of travellers to travel where they wish with an awareness of the social cost of travelling in congested places. Certainly there is no doubt that the most economical way of controlling both pollution and congestion in cities must depend on what the economists call an internalization of the externalities—making the motorist bear not merely the costs of operating his vehicle but the costs of what he does to other people.

Under present circumstances, Mr Ruckelshaus and the American Administration as a whole are caught in an awkward dilemma. For one thing, the new cars, whenever they are introduced in 1975 or 1976, will be less efficient and will consume an extra amount of fuel variously estimated to be between 25 per cent and 40 per cent. At a time when the United States is as much concerned with securing its supplies of petroleum for the immediate future as with the quality of the atmosphere in city centres, this is an awkward but significant if unforeseen accompaniment of the emission regulations. That, by itself, might be sufficient reason for a postponement of the regulations *sine die*. Another difficulty is that the United States cannot insist on the rapid implementation of the auto emission regulations without simultaneously increasing the demand for Japanese cars and not the products of Detroit. But is it politically feasible, let alone wise, to incur such an import bill when the balance of payments of the United States with the rest of the world is already adrift and likely to increase negatively in the years ahead still further as imports of petroleum grow? In other words, for all Mr Ruckelshaus's brave words last week, the truth is that the United States cannot afford to implement his regulations. To do so would entail such an increased pace of growth in the trade deficit that the dollar would have to be devalued yet again. The sad truth, in other words, is that the United States has been brought face to face with one of the principal features of any attempt to improve the quality of the environment—that any improvement costs money and that improvements carried out on a crash time table cost still more.

So must the Environmental Protection Agency and Mr Ruckelshaus (while he remains) sit on their hands and hope for the best? Luckily, there are constructive steps that can be taken. First of all, there are potentially great benefits in the proper understanding of the relationship between vehicular traffic and the pollution of city centres and the better understanding of how people may be damaged by specific concentrations of polluting gases. Moreover, such a programme of research could be mounted quickly—parts of it are already well under way—and a year from now enough could be said to make the problem much more tangible than it is at present. Second, there is much that could be done by fiscal means to encourage the production and sale of much smaller

internal combustion engines. It may be true that distances in the United States are, in general, much greater than elsewhere, but city vehicles stand out among those which travel comparatively short distances. So why not identify the characteristics of vehicles which contribute to city pollution—cubic capacity might be one— and then tax accordingly? For the most distant future, however, there are plainly great possibilities in the radical redesign of internal combustion engines with rotary engines and multi-carburettor systems. It has been conventional, in the past few years, to complain that Detroit has neglected these possibilities. It would be much more accurate to say that Detroit has not had time but that the Administration, with its unparalleled access to facilities for research and development in government laboratories, might in the past year or so have sponsored the kind of research that would have allowed Mr Ruckelshaus to know that he was not standing on thin ice and, by judicious licensing of patents, forced Detroit along whatever was eventually considered to be the socially desirable path of innovation. As things have turned out, however, the auto emission regulations will rank with the ban on cyclamates as an illustration of how it is not feasible to conjure up administrative solutions for technological problems by waving a magic wand or even by passing an Act of Congress. To cry for the Moon is permissible only so long as there is a certain scepticism that the product can be delivered.

100 Years Ago
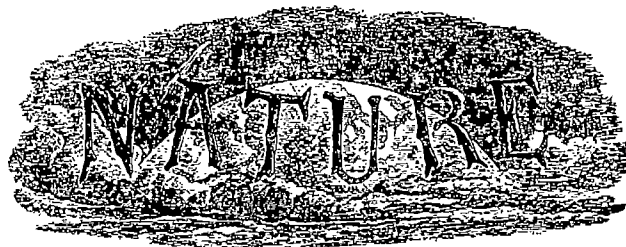
FOR the purpose of more fully carrying out the law of Congress in reference to the propagation of useful food fishes in the rivers and lakes of the United States, the United States Commissioner of Fish and Fisheries made arrangements with Mr. N. W. Clark to hatch out several hundred thousand white fish eggs at his establishment at Clarkston, Michigan, with the special object of transferring them, in due season, to the waters of California. At the proper time, in February last, two hundred thousand eggs were carefully packed and forwarded to California ; but, for some unexplained reason, they were nearly all dead on their arrival. In no way discouraged by this experience, the Commissioner directed the shipment of a second lot of two hundred thousand eggs, which arrived in good condition, and the greater number have since hatched out at the State hatching establishment at Clear Lake, into which body of water they will be put at the right time. The feasibility of shipping the eggs of white fish over so great a distance has now been satisfactorily solved, and there will probably be no difficulty in carrying on this work to any desirable extent. Mr. Stone has returned to the East with the view of procuring living black bass, eels, perch, and lobsters, which he will take back to California in a few weeks, in a special car arranged expressly for the purpose. The California Commissioners appear to be fully alive to the interests involved in the multiplication of the food-fishes in their State, and seem disposed to leave no method untried to accomplish this desirable object.

From Nature, 7, 470, *April* 24, 1873

OLD WORLD

Which Way Forward for Spanish Science?

by our Special Correspondent

SPANISH science is entering a phase of self criticism and reappraisal. In an unprecedented move to help the scientists and the science policy makers in the country, the association of scientists who work for the Spanish Higher Council for Scientific Research (CSIC) called a meeting in Madrid last week to which scientific luminaries from all over Europe, the United States and Japan were invited.

Apart from organizational difficulties, the Spanish problem is one of where best to concentrate its limited resources for research. Traditionally in Spain, research has been carried out within research institutes, which are in most cases divorced from the universities, and it is only in the past decade that pure research within the universities has been accepted.

A close look was taken at the conference of the way in which Japan has developed since the Second World War. Professor Kankuro Kaneshige of the University of Tokyo, and a member of his country's Council of Science and Technology which advises the Prime Minister, freely admitted that Japanese progress had come about through the development of discoveries made in other countries. But he emphasized that it was Japanese scientists who had put considerable effort into turning the knowledge into commercial benefits.

The way in which France organizes its scientific activity was presented by Mr Philippe Richer, assistant to Mr Pierre Aigrain who now holds the position of scientific adviser to the French Prime Minister.

The comparatively inflexible way in which France organizes its research effort contrasted sharply with the methods by which Britain, with no minister and no overall policy for research and development, organizes its research. Sir Brian Flowers stoutly defended the British way—including the customer-contractor principle — and asked the meeting to decide whether the British system is "an untidy mess or a good example of British pragmatism".

But which way should Spain go? Should it follow the lead of Japan, which was universally agreed to be good for a country in the short term, or should it aim at a longer term solution by building up basic research within universities or research institutes? Or, indeed, should the resources available be somehow divided between these two approaches?

The eagerly awaited contribution to the debate by Mr José Lladó, the deputy president of the CSIC, lost some of its impact when the talk had to be read because of his sudden illness. But the audience was highly pleased with the contribution of Mr Federico Mayor, recently appointed acting president of the CSIC who, as well as revealing the philosophy behind his direction of the council, stressed that in future the research institutes and the universities will have to move closer together.

Professor Isidor Rabi, of the University of Columbia, reminded the audience of the meteoric rise of science in the United States in the late 1920s and 1930s—not, he said, because of any

EARTH RESOURCES
Skylark's Eye View

THIS near infrared photograph of some 300,000 km^2 of Argentina was taken by a Skylark rocket on its first operational use as an Earth resources survey. The photograph, one of 650 taken during two Skylark flights in late March, shows an area to the east of the Andes in the south of the Cordoba province from a height of 200 km. Cloud to the right of the picture hides the Andean foothills from which a number of rivers flow, and the different tones of the fields indicate the various types of crop that are being cultivated. A town can be seen clearly in the centre of the photograph with roads leading to it. The Skylark's rocket body, which separated from the payload 57 seconds after launch, can be

conscious policy decision but because a lack of restriction encouraged scientists to work hard. Professor Philip Abelson, President of the Carnegie Institute and editor of *Science*, outlined a depressing view of the United States scientific scene. But he gave a bouquet to Bell Laboratories and held it out as a model of "scientific openness". But Professor Abelson was highly critical of the massive increase in cancer research funding that President Nixon announced last year. "Most of the money spent in the United States on cancer research will be wasted," he said.

But in spite of national differences in approach to science and different scales of scientific activity, all the representa-

seen falling away in the top left of the picture.

The survey will reveal land use and provide crop inventories of Argentina's chief agricultural region, and the photographs are currently being analysed by members of the University of Reading's Geography Department and Argentina's Instituto Nacional de Technologia Agropecuaria.

The next use of Skylark as an Earth resources rocket will be in northern Sweden this summer when a vegetation survey will be attempted. The chief advantages of using Skylark for Earth resources are said to be cost (launch only costs between £100,000 and £150,000) and the fact that launch can be delayed until cloud conditions are perfect—as happened in the Argentinian survey.
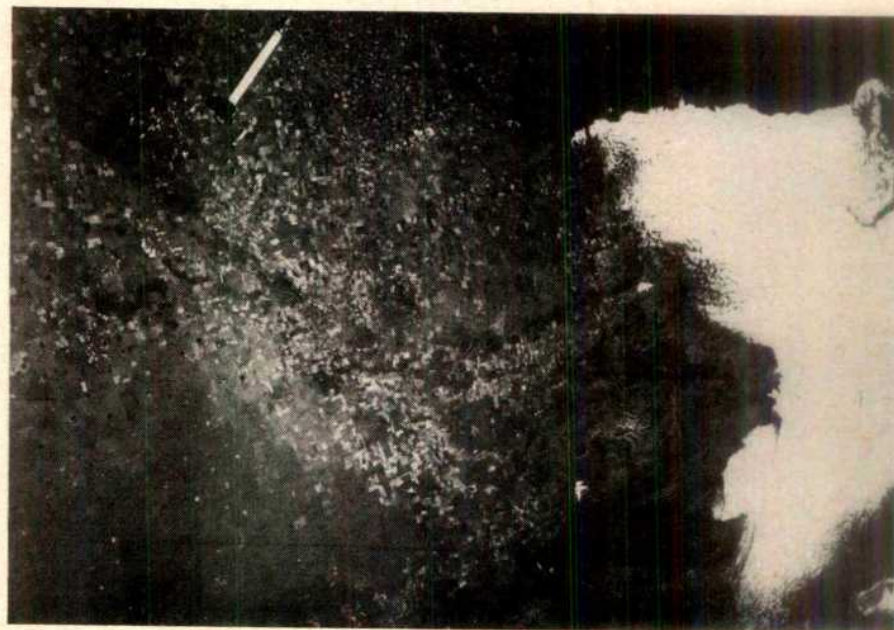
tives when asked were in agreement that Spain must make its own mind up on how to frame its science policy. There was plenty of food for thought for Spanish scientists and science policy makers at this meeting. It now remains to be seen whether it is digestible.

LINEAR MOTORS
We Shall Overcome

A NATIONAL centre to study electrically propelled surface transport is to be established by Imperial College, University of London. This is the reply of Professor Eric Laithwaite and his colleagues at Imperial College to the recent government decision to cancel the tracked hovercraft project (see *Nature*, **241**, 492 ; 1973).

Professor Laithwaite, appearing before the Select Committee on Science and Technology last week, ridiculed the government's plans to continue research on linear motors through a joint programme of work between the National Research Development Corporation (NRDC) and Hawker Siddeley, with British Rail studying the problems of magnetic suspension.

Hawker Siddeley, said Professor Laithwaite "will be starting from scratch" in this type of work and he cannot understand why the government chose this company in preference to others, in particular GEC or Linear Motors Ltd of Loughborough, which already have expertise in linear motors.

Professor Hugh Ford, also of Imperial College, outlined to the select committee the reasons why it is essential to set up a national centre for this type of work. Britain must maintain its lead in linear motor technology and for this to be done the efforts of the universities and industry must be coordinated. Professor Ford was adamant, however, that the present scheme is not an effort to resuscitate Tracked Hovercraft Limited although an essential part of the plan is to use the test centre which THL has constructed in Earith.

Both Professor Laithwaite and Professor Ford stressed that research into surface transport using linear motors has to be done with a full scale track. As this is already available at Earith it is the natural place to site the proposed centre.

The plan is to fund the proposed centre with money from the research councils, universities and industry. Money will be sought both in Britain and abroad. A permanent staff at Earith of about 30 people is envisaged (Tracked Hovercraft Limited employed more than a hundred). Imperial College will play a large part in running the centre simply because it is recognized that the expertise that the college has in transverse flux motor design and electromagnetic levitation is far more

advanced than that found anywhere else. The centre will be a contract research organization that will, according to Professor Ford, assist the British linear motor and magnetic suspension programmes.

But the select committee could not allow this opportunity to pass without delving further into the government's decision to stop supporting THL. Professor Laithwaite admitted that he was not formally consulted on the closure of Tracked Hovercraft Limited although he modestly admitted that he is the world's leading expert on linear motors. Neither the Department of Trade and Industry, the Department of the Environment or British Rail had asked his advice on this matter although he

Professor Eric Laithwaite.

had discussed it with a representative of the National Research Development Corporation. British Rail, said Professor Laithwaite "does not want to know me", as it is firmly wedded to the idea of steel wheels on steel rails.

British Rail is committed to the Advanced Passenger Train moving along existing track at 150 mph but Professor Elliot of the City University, who also appeared before the select committee, expressed severe reservations about the APT. There are two chief problems, said Professor Elliot. First, it is doubtful whether the track can be maintained to the standard necessary to carry trains at such speeds and, second, it is questionable whether the train will make efficient electrical contact with the live rails at 150 mph.

But Professors Elliot and Laithwaite cast a more serious doubt on British Rail's plans by challenging the basis of BR's decision to base the future of high speed transport in Britain on trains running on existing track, thus avoiding an expensive track building programme. How can the present intensity of slower

speed rail traffic be compatible with the APT, they asked? A train intended to run from Manchester to London in an hour will need a clear run, so where will the freight and other traffic go? The only solution, according to Professors Laithwaite and Elliott, is to build new track for the high speed trains. This removes the chief argument for persisting with British Rail's steel wheel on steel rail policy.

In a carefully phrased set of questions Mr Ted Leadbitter got Professor Laithwaite to relate details of a conversation he had with Dr Ieuan Maddock, chief scientist at the Department of Trade and Industry, after Dr Maddock had been shown a demonstration of the work of the Imperial College group. At the end of what had obviously been an impressive demonstration Professor Laithwaite said that Dr Maddock "clenched his fist and said I wish that I had known all this sooner". The demonstration took place on February 5 of this year. The decision to cancel the Tracked Hovercraft work was reportedly taken in January although it was not made public until February 14.

NUCLEAR STRUCTURE FACILITY
Enquiry Holds Up Work

THE Department of the Environment has called in the scheme to build a nuclear structure facility at Daresbury and a planning enquiry is to be held. This unexpected move by Mr Geoffrey Rippon's department could hold up construction for several months.

Professor Alick Ashmore, Director of Daresbury, the Science Research Council's nuclear physics laboratory, said this week that he was surprised by the department's decision, particularly as Cheshire County Council, within whose area Daresbury falls, had willingly supported the planning application in February. "If the plans had been called in before then," Ashmore said, "I would not have been surprised, but at this stage it is rather unexpected."

Assuming the enquiry allows the SRC's plans to go ahead, Daresbury will have a 20 to 30 million volt electrostatic accelerator by about 1978. The project, which the SRC approved in January, will cost £5 million over four and a half years, and will provide Britain's nuclear structure physicists with a low energy accelerator that they have waited ten years for already (see *Nature*, **237**, 192 ; 1973).

Professor Ashmore said that having the plans called in is bound to produce a delay. "We can carry on with general research and development on higher voltages," he said, "but we can't start to build." Work is also being held up by the Department of Education and Science, which has still to give the SRC permission to spend the £5 million.

NEW WORLD

Auto-Emission Standards Postponed

by our Washington Correspondent

MR WILLIAM D. RUCKELSHAUS, administrator of the Environmental Protection Agency, last week sacrificed the Federal Government's plans to clean up city air for the financial wellbeing of the corporate giants of Detroit. That, at least, was how spokesmen for several environmentalist organizations greeted his decision to grant car makers an extra year to produce vehicles which meet stringent standards for exhaust emissions. But spokesmen for the corporate giants take a different view of Mr Ruckelshaus. They have accused him of putting thousands of jobs in jeopardy by drawing up a new set of emissions standards which are still impossible to meet on time.

By any measure, the decision which Mr Ruckelshaus was forced to take last week was a vexed one. In short, he had to decide whether or not car manufacturers are capable of making 1975 model cars which emit 90 per cent less carbon monoxide and hydrocarbons than those produced in 1970. If he decides that they cannot, he is allowed by law to grant them one year's grace and to set fresh standards for 1975.

At stake, Mr Ruckelshaus pointed out, are billions of dollars, hundreds of thousands of jobs, the single most important segment of the US economy, the largest aggregate manmade contributor to air pollution and the ambivalence of the American public's intense drive for healthy air and apparently insatiable appetite for fast, efficient and convenient automobiles. He might have added to the list the future of the Clean Air Act.

A year ago Ruckelshaus decided, on the basis of a lengthy set of public hearings, that the technology for meeting the emissions standards would be available by 1975, and he denied the car makers' request for a year's extension. But he was forced by an Appeals Court ruling in February to re-examine his decision and after yet another set of hearings he backed down and granted the request. But no champagne corks were popping in Detroit in celebration, because Ruckelshaus has set stringent emissions control standards for California in 1975 —which will force manufacturers to fit emission controls to cars sold there— and standards for the rest of the United States which go half way towards the original 1975 standards.

What caused the EPA administrator to change his mind? The most important factor was the Appeals Court ruling which allowed him to bring considera-

tions of social and economic impact on the automobile industry into his decision. Another was a report drawn up by a committee of the National Academy of Sciences which suggested that if the 1975 standards were adhered to, the manufacturers would be forced to adopt what the committee considered to be bad technology, and a third factor was that several Japanese car makers have stolen a march on their American competitors by bringing out an engine which is capable of meeting the standards and which looks a better bet in the long run for ensuring that city air is cleaned up.

The essence of Ruckelshaus's decision involves the question of whether or not oxidation catalysts fitted to car exhausts will work and whether or not car makers can install them in time. US automobile manufacturers opted at an early stage to keep the conventional piston engine and to try to clean up the exhausts with platinum catalysts, but some Japanese manufacturers took a more radical approach which looks like paying off. They intend to fit their cars with stratified charge and Wankel engines, and in fact Honda and Toyo Kogyo have already produced test vehicles which meet the 1975 standards with ease.

The committee of the National Academy of Sciences reported in February that the catalyst would probably work but said that it is less reliable, heavier on fuel and generally a worse option than the stratified charge engine. Ruckelshaus was therefore faced with the following choices. Either he could force all US manufacturers to comply with the 1975 standards on time, in which case they would have no alternative to using catalysts, or he could relax the standard in the hope that car makers would use the extra year to switch to other engine designs, but that is generally considered unlikely. A third alternative, and the one he eventually chose, would be to force manufacturers to fit catalysts on some of their cars in 1975 and to ensure their widespread use in 1976.

His decision will force manufacturers to fit catalysts to all 1975 cars sold in California—which represents about 10 per cent of the US market—and to all their 1976 models. Ruckelshaus took that course because he believes that "the oxidation catalyst is workable and the catalyst is the technology which must be used if the statutory standards are to be met by 1975 or 1976". In other words, since the US manufacturers put all their eggs in one basket by opting for cata-

lysts rather than by engine redesign, their only hope of meeting the standards —even if they are deferred for a year— will be with catalysts.

By forcing manufacturers to phase in catalysts over two years rather than insisting that they be used on all 1975 models, Ruckelshaus said that he is attempting to avoid widespread social and economic disruption in the car industry. But he is also concerned to prevent the Clean Air Act from being torpedoed from Detroit.

If Ruckelshaus had stuck to the 1975 deadline, it would be a foregone conclusion that the car makers would quickly come running to Washington to see their congressmen and senators in an attempt to alter the Clean Air Act and their potential for blackmail would be immense. They would simply say that their production lines would not be able to fit catalysts in the time allowed, that production of cars would have to be curtailed, hundreds of thousands of people would be laid off and Detroit would be turned into an economic disaster area. Backed by a nation-wide advertising campaign, such arguments would swiftly bring Congress round to Detroit's way of thinking.

In steering a middle course between Detroit and its critics, Ruckelshaus may have succeeded in blunting some of the car makers' arguments for repealing or cutting a wedge into the Clean Air Act, and the EPA hopes to show that the economic dislocation caused by the two-phase introduction of catalysts will not be great.

But Detroit is already girding its loins for battle and it will wage war on two fronts. First, it will argue that the interim standards that Ruckelshaus has set for outside California cannot be met without the use of catalysts, and second, it will attack another provision of the Clean Air Act, namely that emissions of oxides of nitrogen must be reduced by 90 per cent by 1976. To help in its campaign, the manufacturers have already engaged the help of their bedfellows in the oil industry whose interest stems from the fact that exhaust catalysts will require unleaded gasoline which the oil companies do not want to provide.

A taste of the possible campaign was given last month when full page advertisements were taken out by car makers pointing out the costs of emissions controls and the fuel penalties that will fall on the owner. An advertisement from the Mobil Oil Company, for example, called the Clean Air Act "a

66 billion dollar mistake". Not to be outdone, however, the Sierra Club responded with an advertisement urging Ruckelshaus to hold fast on the 1975 deadline.

As for the manufacturers' first point, Ruckelshaus stated last week that "the technological information available to me indicates that few catalysts will be required to meet this standard". But the manufacturers chorused that their information leads them to a different conclusion, and they hinted that they may take their case either to the courts or to Congress.

But as far as the standards relating to oxides of nitrogen are concerned, they may be on firmer ground and in any case they are likely to have the backing of the EPA. In short, the EPA has set a limit of 100 micrograms of nitric oxide per cubic metre of air as the maximum level to protect health and it originally estimated that the limit is exceeded in 45 regions throughout the United States. But it has since re-evaluated the concentrations using more precise techniques and will soon disclose that the level is exceeded in only two regions—Los Angeles and Chicago. Ruckelshaus in fact said last week that "our assessment of the health risk associated with (oxides of nitrogen) no longer supports the 90 per cent reduction standard and this should be reviewed quickly and, if our analysis is correct, the standard should be changed".

The automobile companies would be delighted if Congress accepts the need to change the standards because they have not yet found a reliable method for reducing emission of oxides of nitrogen. So far, US companies are concentrating on a dual catalyst approach but the NAS committee said in its report that no system has yet been found to be reliable and that the dual catalyst has a huge fuel penalty, increasing gasoline consumption by up to about 25 per cent. The stratified charge engine developed by Honda seems capable of meeting the standard for oxides of nitrogen as well as those for hydrocarbons and carbon monoxide, however.

The reason why the EPA is anxious to protect the Clean Air Act from being butchered is that it involves regulation of many sources of pollution in addition to automobiles and that changes in one area will affect others. The act requires the EPA to set ambient air quality standards nationwide and the states are empowered to meet the standards according to a specified timetable based on the emissions standards now established. But if the car makers are given more time to control exhaust emissions, many of the states' plans for meeting the air quality standards could be thrown badly out of kilter.

In the final analysis, however, the US car makers have only themselves to blame if they end up using inferior technology to curb exhaust emissions. They began to work seriously towards pollution control only when the Clean Air Act put a pistol to their heads and, unless they can now bully Congress into giving them a second chance, they may have to pay for their mistakes on the market place when they compete with the Japanese companies.

ENERGY RESEARCH

Rumblings from Congress

by our Washington Correspondent

ALTHOUGH statements, reports and recommendations on the so-called energy crisis are by now two a penny, a report published last week by a special congressional task force merits careful reading. It suggests that spending by government and industry on research and development on new sources of energy has been unbalanced and insufficient, and calls for at least an additional $1,000 million a year. The report is important because the task force which produced it has recently been promoted into a full subcommittee of the House Committee on Science and Astronautics, and as such will have a strong voice in shaping legislation dealing with energy research. It is also a useful yardstick by which to measure President Nixon's long overdue and eagerly awaited statement on energy policy, originally promised for February and now expected to be unveiled this week.

In short, the task force, which met under the chairmanship of Mike McCormack, an energetic young congressman from Washington, took a careful look at a report prepared for President Kennedy in 1964 by an inter-agency committee, and concluded that most of its recommendations "are still valid today—valid because so little action has been taken to implement them". The task force also recommends that an energy policy group should be established in the White House and that all the energy programmes of the Federal Government should be centralized in a single agency.

The task force does not say exactly how the extra $1,000 million should be spent, or how it should be divided between the Federal Government and industry. But it does suggest that past spending has been biased towards nuclear energy, and singles out seven priority areas which hold great promise and deserve more money. They are basic research—for example, the National Science Foundation's RANN programme—materials science, solar energy, geothermal energy, breeder reactors, coal gasification and liquefaction and controlled thermonuclear fusion. Of these, only the breeder reactor has been given high priority by the Administration, and then the money has been put into the liquid metal fast breeder almost to the exclusion of other designs.

The suggestion that an extra $1,000 million should be spent on energy research and development is based on the task force's belief that 10 per cent of the total national research and development effort should be devoted to energy. Given the technologically intensive nature of the energy industries, such an expenditure is not unreasonable, the task force states, since total outlays on research and development in the United States are running at a little under $30,000 million. Such a commitment would require about $3,000 million to be spent on energy research. But only some $2,000 million is expected to be spent next year, and of that about $750 million will come from the government.

Viewed in conjunction with the energy research and development programme proposed by Senator Henry Jackson and several of his colleagues (see Nature, **242**, 224 ; 1973), the task force's proposals indicate which way the wind is blowing on Capital Hill. Jackson's bill calls for expenditures by the Federal Government of $2,000 million a year over the next ten years on non-nuclear energy research.

Meanwhile, President Nixon's budget for next year calls for only $772 million to be spent on energy research and development, and in view of the Administration's present cost-conscious mood, the forthcoming energy message is not expected to add much more money to the budget request. Funding for energy research is thus likely to be yet another bone of contention between the White House and Congress.

Erratum

THE photograph that inadvertently appeared on page 364 of this volume of Nature was, of course, of Britain's Goonhilly 3, a £2.25 million satellite communication station which was opened last July. The 158-inch Mayall Telescope that should have appeared is pictured above.

NEWS AND VIEWS

The Screw Worm Strikes Back

THE eradication of the New World screw worm, *Cochliomyia hominivorax*, first from Curaçao and then from the continental United States through the release of factory-produced sterile flies can be counted a scientific and an economic success both from the novelty and acceptability of the method and from the rapidity with which the losses suffered by the American livestock industry were overcome.

The danger of re-invasion from uncontrolled Mexico, however, required a permanent, continuous "barrier" of releases extending some 250 miles in width along the 1,500 miles of the USA-Mexico border. During the operation of the scheme practical imperfections in this barrier became evident. These stemmed from (a) the limited capacity of the single, permanent sterile fly-factory at Mission, Texas (producing approximately 100 million sterile flies of both sexes per week); (b) the flight range of the female screw worm fly (up to 180 miles) (B. G. Hightower, in *Insect Ecology and the Sterile-male Technique* (Proc. Panel, Vienna, 1967), 25 (IAEA, Vienna, 1969)); and (c) the length of the USA-Mexico border.

International and domestic cooperation in monitoring screw worm activity in the barrier area with a view to gauging the density and spatial pattern of aircraft release of sterile flies has been used to offset these imperfections, and it was initially successful. Recently, however, there has been a major setback, judging from the published figures in the weekly *Cooperative Economic Insect Report*

Fig. 1 Cases of screw worm and releases of sterile flies, 1972, per week, United States and Mexico (data from the *Cooperative Economic Insect Report*, US Department of Agriculture). ●—●, Releases (thousands) in the United States; ○—○, releases (thousands) in Mexico; ——, cases in the United States; ●- - -●, cases in Mexico.

published by the United States Department of Agriculture (see Fig. 1 and Table 1).

Table 1 Confirmed Cases of Screw Worm, USA and Mexico

	1962 *	1969 †	1970 †	1971	1972 ‡
United States	50,000	219	153	473	92,192
Mexico §	—	—	4,634	8,811	27,467

Data summarized from the *Cooperative Economic Insect Report*, US Department of Agriculture.
* Estimate.
† "Lowest 2 years ever."
‡ December 18, 1971, to November 18, 1972, except May 14 to 27.
§ As most of these cases were reported from the "barrier zone", the totals for Mexico are likely to be gross underestimates.

In 1962, after a successful eradication scheme in Florida, the United States south-west project was launched. By 1966 only small numbers of cases of livestock infection could be detected, with an all-time minimum of 153 in 1970. The rise to 473 in 1971 was hardly a portent of things to come unless a discerning eye could attach some significance to the fact that more than 50 per cent of the cases were registered in September and October rather than earlier in the year. In 1972 a cumulative total of 500 was surpassed in the week of April 17 with the greater part of the spring still to come. Ominously the weekly confirmed cases rose to 609 during the second week of May and a peak of 5,013 was reached at the end of June. During July the tide seemed to recede, but by the end of August the 5,000 mark was almost touched again. A slow decline, probably reflecting the season, followed, but more than 3,000 per week were being recorded by the end of October. As 92,192 cases could be counted from December 18, 1971, to November 18, 1972, the estimate for 1962 (50,000) was surpassed, though it should be pointed out that nowadays in the United States case finding and reporting are more efficient than in the past.

At present it is not known exactly why the screw worm returned. A possibility is that there has been a behaviouristic selection for assortative mating which has diminished the efficiency of the factory-produced sterile males. In other words, there may have been an increase in the likelihood of a wild fly being mated by a wild fly rather than a sterile one, given an equal choice. If this is the explanation one wonders whether the regular incorporation of fresh, wild material into the sterile-fly factory could increase the efficiency of the releases. Perhaps the selection inherent in colonization and mass rearing also affects the mating behaviour independently of any direct effect of the sterilization operation.

In response to this return of the screw worm the number of sterile flies released was doubled to about 200 million (half of them males) per week during 1972, but this increase was obviously insufficient because the reported
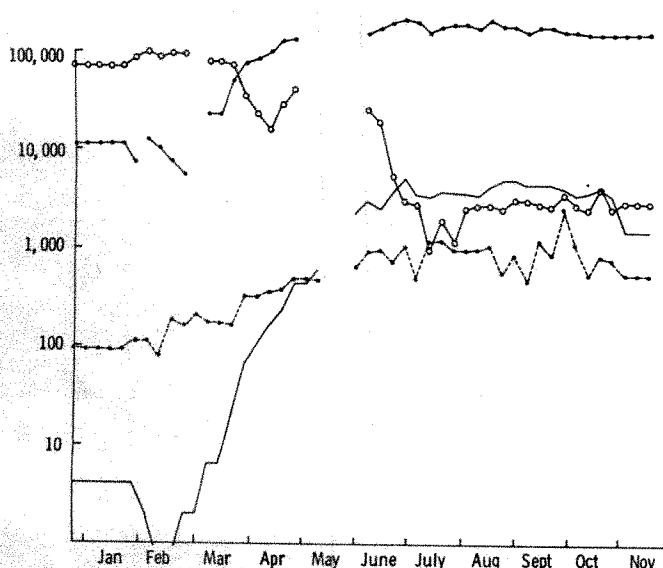
number of screw worm cases in the United States followed a familiar seasonal pattern. Concomitantly, as the pest spread back into the originally infected (receptive) areas of the United States, both the relative and the absolute number of sterile flies released over Mexico declined. On Ocober 29, 1972, a press release in Mexico City specified that following an agreement with the United States government a 5-year nationwide screw worm eradication effort would start during November and would involve the building of a sterile-fly factory at Salina Cruz in the Tehuantepec Isthmus with a capacity of 300 million sterile males (probably weekly). This suggests that the barrier would eventually be in the waist of Mexico, as proposed by Hightower and Graham (in *Control of Livestock Insect Pests by the Sterile-male Technique* (Proc. Panel, Vienna, 1967), 51 (IAEA, Vienna, 1968)) (see Fig. 2) though it has already been suggested by Bushland (in *Sterility Principle for Insect Control or Eradication* (Proc. Symp., Athens, 1970), 3 (IAEA, Vienna, 1971)) that a better, more logical place would be in Panama and Costa Rica, where Central America narrows to a width of less than 100 miles for hundreds of miles.

Besides the barrier problem there is the formidable task of re-eradicating the screw worm from the United States. Even with the help of the weather, a principal factor in determining the size of the overwintering area, which is much smaller in comparison with the summer receptive area, it seems doubtful whether the screw worm could be quickly beaten back to the 1970 level with the present material, procedures and logistics.

Assuming, optimistically, that increased numbers of factory-produced sterile flies are all that is needed, hope comes squarely to rest on the projected Mexican, Salina Cruz plant (if the Mission, Texas, plant is not expanded or duplicated elsewhere in the United States). Its sterile flies could then supplement the releases in the United States or could be used independently, working northwards, after securing the Tehuantepec barrier. The eradication of the fly from Mexico, however, also presents potential difficulties in the way of: (a) mountainous terrain and difficult communications; (b) a relatively very small area subject to winter conditions inimical to screw worm survival; (c) higher density, compared with the United States, of livestock in general and in particular of sheep and goats (considered better hosts for the fly);

(d) absence of large livestock ranches with unified management; and (e) constant livestock movement towards the central consuming centres from and through the Tehuantepec barrier. Furthermore, the tropical moist conditions of some of the livestock areas of Mexico in the Tehuantepec barrier or further to the north may well require different procedures and/or release ratios in excess of those which have been found sufficient in the United States. At present, however, it is not at all certain whether increases in the weekly figures of releases of factory-produced sterile flies in their present form are the answer required. Until this matter is settled by adequate research or by a succesful re-eradication from the United States it could be wasteful to attack the tropical habitats of the fly. It is now known that both Mexico and the United States have set aside $40 million to be spent on the eradication of the screw worm during the next 5 years and on the establishment of a barrier zone.   C. B. C.
                                                                                    D. M. B.

Knack or Knowledge ?

THE transistor was invented twenty-five years ago and the stir created by its anniversary has now abated a little. Having heard in full about the benefits which that invention has provided (see, for example, *Nature*, **242**, 91 ; 1973), it is perhaps time to consider a weakness which appears in the successors of Bardeen, Brattain and Shockley—one which they studiously avoided — namely the tendency to use knack rather than knowledge to achieve difficult goals in solid state technology. Unfortunately many impatient men in the massive solid state component industry try to run before they can walk, with the results that usually attend such overconfidence.

The transistor has endowed tremendous scope for performing electronic functions (for example switching, which permits binary logic, and amplifying, which makes possible many other forms of signal processing). The chief advantage over the valve is the ability to perform those electronic functions within very small volumes of solid. For example, a switch may occur roughly 100 μm^3, which should be compared with the volume of a pinhead—many millions of μm^3. The smallest conceivable valve device may be several times larger again. As a result one can now, with some ease, put a minicomputer on a postage stamp (the 'Intel' silicon microprocessor integrated circuit is actually about 1 cm on a side).

For several reasons, however, semiconductor technologists are still trying to get the minicomputer, metaphorically, onto the pinhead. This is not, of course, only showmanship. If this density of electronic functions can be achieved, solid state shift registers may replace magnetic tape recorders and solid state random access memories will have such large bit densities that, to quote a punning headline "Magnetic Cores Will Be . . . Just a Memory". The problem lies in the fact that technological skills are not advanced enough to achieve the densities of function which these commercial ambitions demand. Knowledge of the processes which go into making high density integrated circuits is not accurate enough. Integrated circuits may be mass produced but their preparation involves several intrinsically complex processes, such as impurity
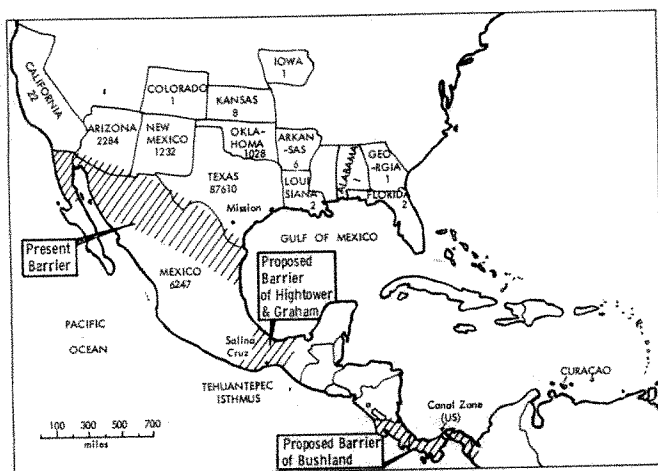
Fig. 2 Cases of screw worm, 1972, and barriers (data from the *Cooperative Economic Insect Report*, US Department of Agriculture).

diffusion in the solid, thermal oxidation of surfaces, pyrolysis of gases and evaporation of compounds. On the whole, industrial scientists have limited themselves to characterizing the broad features of these processes, for example the temperature dependence of diffusion and the dependence of resistivity on impurity concentration. The intense competitiveness of the semiconductor industry has generally made the same scientists stop short of the more fundamental questions of mechanism. For example, it is not well established whether diffusion of dopants occurs by way of vacancies or by dislocation climb (Peart and Newman, Institute of Physics Conference Series No. 6, 170; 1973); and knowledge of the structure of the thermally-grown and deposited dielectric layers, used both as diffusion barriers and electronic barriers in planar silicon technology, is rudimentary in the extreme (see Revesz, *J. Non-Cryst. Solids*, **11**, 309; 1973).

An optimist would say that such fundamental knowledge is not necessary in order to achieve an industrial production process; the right collection of recipes for temperature, time, input materials and so on should permit a limitless number of batches of an established device to be made with good repeatability and high reliability of product. In practice, this repeatability is achieved, if at all, by dint of long struggles and empirical means and the industry suffers seriously from this lack of predictability. It is perfectly common for some uncontrolled variable to change and for the yield of a production run to fall far below a commercially acceptable level. Everybody in the industry has a story of a production line which "lost the knack" for a few weeks. This applies to processes other than transistor preparation, of course, and other industries may have helpful lessons to teach. The situation in the solid state industry simply seems to be that skills are being stretched too far; that in the manipulation of solid state phenomena to the dimensional accuracy demanded today much better predictive formulae are needed to foresee the influence of, say, slight changes in starting materials on the dimensions and electronic transport properties of the final melange of atoms which constitutes the desired electronic function. The director of the research laboratory of an electronic company recently said publicly that knowledge of the solid state phenomena used, compared with what one needs to know, is "pathetic" (*Nature, loc. cit.*). How, then, does one keep knowledge of the physics of processing matched to the demands? The same speaker ruefully admitted a gap in the research machinery and an accompanying sense of frustration in trying to fill that gap. He felt that the traditional venue for accumulating fundamental knowledge, the university physical laboratory, was not, as constituted now, well matched to the task in the case of the relevant solid state phenomena. On the other hand, he admitted the common difficulty of persuading semiconductor manufacturers to support the work of their own laboratories.

At this stage, one should examine several general features of the problem. First, the research goals are of a type often termed "underlying research", although the problem is perhaps more acute than many tackled under this heading. Second, the problem at present chiefly concerns silicon device technology; certainly all facets of the problem are expressed in this global industrial common factor. More is known about this semiconductor than any other and still the problems obtain; thus, what applies to this material will probably apply to others.

Third, although the problem affects nearly all manufacturers of semiconductor devices, their nearness to the problem may, in fact, give them the wrong perspective on how to treat it as a whole. Industrial laboratories are usually better at developing improved designs or new principles for devices (a more glamorous and profitable business than cleaning up behind themselves) and hence may not see that filling certain gaps systematically is "for their own good". The extent of the physical problems is so wide that at least a national scale is required for their investigation. Thus, the venue of such research should lie between the universities and government establishments, with national coordination. The national need which will most directly benefit from the research will be trade, although defence will also be a principal beneficiary. The benefits may be greater than for most underlying research.

In considering the particular failings of the university in this context, it is clear that the carrying out of research through the medium of graduate students is not well matched to the rigorous requirements of purity and accuracy in research on solid state processing. Continuity in skills and immense care in control of process conditions have been found to be the only answer to repeatability of results in this field. The necessary continuity could perhaps be provided within a university by the provision of a permanent staff more than usually committed to this continuity. This is the intent, it seems, of the several Materials Science Institutes set up in the United States in the 1960s. The disciplines needed are physics, chemistry, metallurgy and general engineering skill. Some departments of electronic engineering, in fact, already pursue approximately the right combination of topics. Government research laboratories have the right degree of stability, but the trend is now towards the project approach. Except, perhaps, in the laboratories interested in standards and metrology, the acceptance of an appeal to a general, underlying improvement may not be easy to find. It is significant that the chief establishments for electronic materials research are under the control of the Ministry of Defence and have well defined but narrow objectives.

As to finding money for such work, the usual arguments for government support of "high technology" apply here, probably more forcibly than usual. It might even be argued that institutes developing an understanding of the physics of processing would be likely to pay for themselves directly in licences and indirectly in the benefit accruing to the nation concerned in terms of efficiency—money saved by the avoidance of setbacks and of waste—and in terms of national trade improvement as semiconductor products become more competitive in the international market. It could be objected that the British government already su'ports such work in such programmes as the Compo and Valve Development and Computer Technolo' ject. As the titles of these activities suggest, each programme is essentially looking for te produce devices of higher performance, rath' ing for the principles behind consistency moreover, the ultimate uses of devices defined and the required generality of commitment may be missing. W' improvement in the accuracy ac processing. Cookery is not enoug. economically better than knack.

MEMBRANES

Argument

from our Molecular Biology Correspondent

A SYSTEM that has done service as an archetype for the structure of biological membranes is the retinal rod outer segment. A feature that especially commends it for such a role is that it contains only one protein in large quantity. After some early skirmishing the X-ray practitioners appeared to reach general agreement about the electron density profile across the bilayer, and more particularly in the conclusion that the electron densities, given the proportions of rhodopsin and phospholipid in the membrane, could not be made to add up for any model embodying protein totally submerged in the bilayer, or plating the surfaces, and were best compatible with globules floating, only partly immersed, in the membrane fluid.

Last year Dratz and his colleagues (*Nature New Biology*, **237**, 99 ; 1972) attempted to shatter this tranquil accord by arguments based on chemical labelling experiments in intact rod outer segment membranes compared with the isolated rhodopsin. In this they seem to have been wrecked on a reef that has accounted for many a good protein chemist in its time, and now familiar to most, namely that the reactivity of side chains in proteins is controlled by a variety of factors besides mere steric accessibility. The plan was to use a macroscopic labelling reagent, which would be unable to enter the bilayer, and could therefore modify only groups exposed to the aqueous exterior. The reagent in question was fluorescein isothiocyanate adsorbed on a colloidal particle, which was found to react abundantly with rhodopsin, free or in membranes that had been broken up with detergent or a phospholipase, but not in the intact or even sonicated membrane. From this they boldly inferred that the rhodopsin *in situ* must be totally buried within the bilayer.

Vanderkooi in this week's issue of *Nature New Biology* (**242**, 212 ; 1973) now points out that this will not wash. Besides the evidence of the phalanx of X-ray crystallographers, he draws attention to the likely role of environmental factors in determining the reactivity of the reactive lysine, tyrosine and cysteine side chains of the protein. It is known that rhodopsin reacts *in situ* with aldehydes, and with thiol reagents : free of the latter, all polar iodoacetmide derivatives, react with one of the reactive thiols of the protein. There moreover, the recent work of Blasie, purports to demonstrate steric in the membrane within a *p*H which only charged groups on in could change their ionization

In their rejoinder Dratz and Schwartz (*ibid.*, 212) seem more concerned with repudiating Vanderkooi's arguments than defending their own position, which they seem in any case to have stealthily evacuated in the interim. The aldehydes, they say, can enter the lipid phase, and react with the protein side chains that they find there. As to the thiol reagents (work reported last year by Wu and Stryer) the results, they assert, prove nothing : two of the reagents have a sufficiently wide separation between the non-polar reactive centre and the polar carrier group that the reaction could occur under the bilayer surface; the third reagent, they believe, might actually be lipid-soluble. Blasie's evidence they counter by questioning whether he has correctly identified an X-ray reflexion that he uses to measure the inter-protein spacing. They have also, they say, calculated Fourier syntheses for the various possible models for the membrane, and whereas some fit the observed electron density profiles in some regards, they fall short in others. This, of course, is not unfamiliar to the crystallographers who have been toiling in the field for some years, and who have recently stressed particularly the complications arising from the structural disorder that is thought to be present. Dratz and Schwartz then come to the point : work of their own and of two other groups, using specific labelling methods in results as yet only available as published abstracts, shows that part of the rhodopsin is indeed exposed to the aqueous medium : the

view that the protein floats partly immersed in the bilayer therefore remains unassailed, and the earlier labelling results were, as one suspected, writ on water.

Also in *Nature New Biology* this week (*ibid.*, 213) is a sequel by Phillips and Morrison to their earlier work on labelling of membrane proteins by a reagent too large to penetrate the bilayer. This is nothing less than a protein, lactoperoxidase, which catalyses the iodination of tyrosine residues. In the red cell, only two proteins are labelled from the outside by this means, one of them the principal glycoprotein, which bears surface receptors for such ligands as plant lectins. As with cells in tissue culture, limited exposure to trypsin results in increased agglutination in the presence of such species, and it has been variously argued that the trypsin treatment leads to exposure of new binding sites, or to increased freedom of the receptor protein to form strongly binding clusters in the membrane. Phillips and Morrison now find that trypsin releases glycopeptides, including one that contains the tyrosines iodinated by lactoperoxidase. In spite of the removal of this reactive residue, the trypsin-treated cells are able to incorporate ten times more label than the untreated, exclusively, moreover, in the same two proteins. These results can be most simply interpreted in terms of the obstruction of much of the surface protein by a fur of carbohydrate, which might well turn out to be a widespread structural feature in membranes.

EB Virus Superinfection of Human Lymphocytes

LINES of human lymphoid cells which multiply indefinitely in culture have, irrespective of their origin, proved to contain Epstein–Barr (EB) virus DNA and EB virus has been implicated in the aetiology of Burkitt's lymphoma and infectious mononucleosis. Cells of many of these lymphoid lines can be superinfected with EB virus even though they contain EB virus DNA.

In *Nature New Biology* next Wednesday (April 25) Adams and Klein report an analysis of the response to superinfection with EB virus of cells of eleven human lymphoid lines, six derived from Burkitt lymphoma tissue and five derived from patients with infectious mono-

Correction

THE article by Riddle and Carbon referred to in a note, "Frameshift Suppressor Transfer RNA", in last week's issue (*Nature*, **242**, 436 ; 1973), will be published in *Nature New Biology* for April 25 and not April 18 as stated.

nucleosis, a patient with leukaemia and from healthy persons. Their findings lead them to the interesting conclusion that either lymphocytes from Burkitt lymphoma tissue differ in type from non-Burkitt lymphocytes, or different subtypes of EB virus are present in the Burkitt and non-Burkitt cells, or the mechanism of transformation of the two classes of cells differs.

Cells of all the lines studied adsorbed EB virus, and one particular stock of this virus proved to be unusually active in inducing viral early antigen. Adams and Klein therefore used this stock to measure the dose response relationship of the Burkitt and non-Burkitt cells. Cells of eight of the eleven lines fell into one of two classes when their dose response curve for the induction of viral early antigen was measured, the non-Burkitt cells having a linear dose response whereas the Burkitt cells had something approaching an exponential dose response. Moreover, three lines, two Burkitt and one non-Burkitt, responded with the production of early antigen much more strongly than the other eight lines.

CHALLENGER SOCIETY

Newcastle Meeting

from a Correspondent

THE opening theme of the joint meeting of the Challenger Society and representatives of marine laboratories, held in the University of Newcastle upon Tyne on March 27 and 28, was the gross estuarine pollution of the north-east coast of England. It is an unhappy commentary that a similar theme characterized a meeting of the Challenger Society at the Dove Marine Laboratory exactly fifty years ago.

Dr J. S. Gray (University of Leeds) has been monitoring Seal Sands in the Tees estuary, an area once indeed sandy and harbouring seals, but now a mud-flat. Nevertheless, in spite of heavy industrial pollution the meiofaunal density of the intertidal sediment here averages 2.5 million organisms per square metre. Dr Gray has found that the species diversity of the annelids of the area is reduced in certain limited stretches; it seems likely that pollution here may reach a peak, yet he is not satisfied that this reduction in diversity can be categorically related to pollution.

Dr A. James (University of Newcastle upon Tyne) described the effects of directing polluting discharges into the Tyne estuary, chiefly in terms of the dissolved oxygen regime, but some mention was also made of intestinal bacteria and nutrient budgets. He showed the results of a one-dimensional model which has been developed to help predict future levels of organic matter, bacteria, nutrients and oxygen.

Dr P. G. Moore (University Marine Biological Station, Millport), taking a more generalized view of environmental quality in the sea, also considered the possibility of using ecological diversity values as indices of pollution. He looked particularly at diversity indices biased towards the equitability component. He has found that although there are problems concerned with varying key species and with the choice of animal size and taxa, the principal difficulty lies not in the measurement of diversity but in its interpretation, so that its use as an indicator of pollution, while possible, requires caution.

Dr R. Johnston (DAFS Marine Laboratory, Aberdeen) returned to specific cases and outlined the problems involved in predicting the effects of a proposed new pulp mill on the chemistry of the waters of two Scottish sea lochs, Linnhe and Eil. A decision whether or not to permit a discharge from the mill into the lochs was required in 1961 although the actual discharge would not begin until 1966. The complexities of the hydrographic situation were unravelled and future changes in dissolved oxygen and bio-

logical oxygen demand (BOD) were estimated and found acceptable. Once the mill was working subsequent routine observation enabled the minor reduction in dissolved oxygen and the minor increase in BOD in the water to be correlated with the BOD and suspended solids input of the mill.

The plankton session was opened by Dr F. Evans (University of Newcastle upon Tyne) who spoke of the long history of plankton sampling in Northumberland coastal waters, extending as far back as 1860 although in a much broken series. The Northumberland plankton does not, he said, derive at all from populations to the south of the county but consists of species constantly found locally, supplemented intermittently by immigrants from the north. This accords with the predominantly southward flow of wind-induced currents close inshore, but it is a matter for remark that species well known only 50 miles to the south are not brought northwards into the region during times of contrary winds and accompanying northerly flow.

A "Challenger" plankton session would seem incomplete without a contribution from Edinburgh, and the demand was met by Dr R. Williams

(Institute for Marine Environmental Research) who gave an account of the extensive sampling programme at Ocean Weather Station "India". The equipment used includes sophisticated sensors of the physical environment combined with a plankton net which incorporates the Hardy–Longhurst cod-end for controlled depth sampling.

Dr M. Sheader (University of Newcastle upon Tyne) dealt with a planktonic group—the hyperiid amphipods of the North Sea—which was previously inadequately known. Of the three North Sea genera, *Hyperia*, *Hyperoche* and *Parathemisto*, he dwelt more especially on the last. His taxonomic studies show conclusively that the large, oceanic *P. gaudichaudi* and the smaller, neritic *P. gracilipes* are in fact the same species; furthermore, laboratory rearing of the young of both forms produces animals which are indistinguishable from each other provided environmental factors are equal.

The plankton session was concluded by Dr S. J. Lockwood (MAFF Fisheries Laboratory, Lowestoft) who reviewed the replenishment of the almost self-contained stock of plaice off the Yorkshire coast. He has found that eggs are spawned some 10 to 20 miles off the

Extraction of Gonadotrophin Receptors

RECEPTORS can be defined as components of a tissue which specifically react with a drug or hormone and which are essential for the expression of the biological activity of the compound. In endocrinology, interest in receptors was renewed about 1960 when it was postulated that specific proteins in tissues of the reproductive tract interact with the sex hormones and are responsible for their uptake by the tissues. Presence of the receptors also explained the specificity of the action of the sex hormones on reproductive tissues. The sex hormones, however, are known to affect metabolic reactions in almost all tissues and presumably therefore proteins which interact with the hormones and which could be called receptors should be present in other tissues as well as those of the reproductive tract. The meaning of "receptor" is becoming very diffuse and a clearer definition of the word is necessary. Receptors which interact with polypeptide hormones have also been shown to be present in tissues; these receptors seem to be membrane-bound and hence their isolation presents difficulties.

In next Wednesday's *Nature New Biology* (April 25) Dufau and Catt describe a procedure for the extraction of gonadotrophin receptors from the interstitial cells of rat testes. After subcellular particles were isolated by centrifugation, they were dispersed in 'Triton'-buffer solution. After extensive high-

speed centrifugation of the solution, gonadotrophin-binding activity was found only in the supernatant solution. Some loss of binding capacity occurred on solubilization, as the final solution had only about one third the binding capacity of the original particles and this was also associated with decrease in the association constant. Thus although all of the receptor may have been solubilized there well may have been a conformational change in the protein. The soluble receptors, however, still appeared to retain their hormonal specificity. Isolation of the receptors by this type of procedure should not only be a great help in their further characterization and investigation of the way in which they function but also enhance their usefulness in the development of methods for assay of gonadotrophins.

A second report, by Milin and Roy, is concerned with androgen-stimulated synthesis of globulin in rat liver. Hep tissue contains a "receptor" whic ultracentrifugation is different f androgen-binding protein r blood. Earlier studies sho sence of this "receptor" ir female and immature Milin and Roy used f a strain of rats wh to androgen bec None of the by ultracentrifuga these animals nor significant amounts of t

Tees. As they develop they drift southwards as larvae and onshore into the north Yorkshire nursery ground. Here, after metamorphosis, the 0 group fish establish a depth distribution related to size. The 0 group over-winter in the nursery ground and begin the migration to the parent spawning ground as 1 group fish.

In her talk on local and annual variations in the recruitment of the limpets *Patella vulgata* and *P. aspera,* Dr R. S. Bowman (University of Leeds) described how, at Robin Hood's Bay, Yorkshire, she chose fixed-site monitoring as being a more sensitive and accurate method of measuring input of settlers than random sampling. Annual input varies widely in both species ; this, she said, seems to result from the effect of summer air temperatures on gonadal development in *P. aspera* and on the susceptibility of newly-settled spat to hard frost in *P. vulgata.*

Dr J. B. Buchanan (University of Newcastle upon Tyne) discussed the life history of the burrowing decapod crustacean *Calocaris macandreae.* A monitoring programme off the Northumberland coast over a ten-year period has shown that this species holds its population density at an average of eighteen individuals per square metre, with a coefficient of variation of only 5.4 per cent. An analysis of grab samples revealed that the species is evenly distributed on the ground and experiments in the aquarium tanks of the Dove Marine Laboratory showed it to defend individual territories which are in the form of burrow systems.

Mr R. Foster-Smith (University of Newcastle upon Tyne) described the effects of turbidity on the feeding of *Mytilus edulis, Cerastoderma edule* and *Venerupis pullastra.* He has found that *Mytilus* is more capable than the other species of withstanding high concentrations of suspended matter, and does this by rejecting a greater proportion of filtered material than either *Cerastoderma* or *Venerupis.*

The special lecture, given by Dr J. A. Allen (University of Newcastle upon Tyne), was also devoted to benthic molluscs but to a group far less familiar than Mr Foster-Smith's cockles and mussels, namely the bivalves of the abyss. Here the bivalve fauna is dominated by the deposit feeding sub-class Protobranchia, whose food consists largely of refractile scleroproteins such as are found in the matrix of the exoskeletons of dead diatoms or Foraminifera. Morphological adaptations invariably include the elongation of the d gut, thus increasing digestion time. wth rate of these animals is very low e life span may be commensurately ometimes in excess of a hundred vith maturity attained at the end fe span.

PHYSICS EXHIBITION

1 + 1 = 2 + ?

FOR the first time, the annual Physics Exhibition, organized by the British Institute of Physics, was held last week at Earl's Court, London, rather than at the more inaccessible, and inelegant, Alexandra Palace. Also, on this occasion the exhibition took place at the same time and in the same place (though on a different floor) as Labex International, an exhibition of scientific instruments.

In the past few years the Physics Exhibition has experienced a disappointing decrease in the number of exhibitors, and at least one of the motives for linking up with Labex International was to try to rectify this state of affairs. Dr L. Cohen, secretary of the Institute of Physics, said last week that the number of exhibitors was about the same as last year, possibly slightly greater. Nevertheless the recent decision to hold the exhibition only every two years from now on still stands.

Several of the exhibits at the Physics Exhibition are traditionally educational in character, and this year one of the most interesting was an inexpensive apparatus for measuring the speed of light. It was devised by the Physics Department of King's College, London, and can be built for about £25 together with the apparatus usually found in school science laboratories (see *J. Phys. E.,* **5,** 1142 ; 1972). The principle is to modulate the output from a gallium arsenide-phosphide light-emitting diode and to compare the phase of this output with the phase of the signal detected at another diode a metre or two away.

Another inexpensive piece of educa-

tional equipment on show was the sound level detector developed for the Technology Foundation Course of the Open University. This is being used by students to measure vehicle and machinery noise as part of their practical work.

One of the more extensive displays was undoubtedly that put on by Harwell to illustrate the many facets of research in which that establishment is now engaged. Among the activities publicized were research on multifilamentary Nb_3Sn superconductors and the work of the establishment's non-destructive testing centre.

Although the a.c. linear motor is now quite celebrated for its role in high speed transport, d.c. linear motors are less well known even though they have important advantages in the context of, for example, machine tools. In such a motor built at the Wolfson Centre for the Technology of Soft Magnetic Materials by the University of Wales Institute of Science and Technology and shown at the exhibition, the field excitation is provided by ferrite permanent magnets and the armature is a steel bar wound with copper wire. The speed of the motor can be varied simply by altering the current flowing through the armature.

Time alone will tell to what extent the next Physics Exhibition in 1975 will benefit from the decision to hold the event less frequently. It is certainly true to say, however, that many people who have not visited the exhibition every year in the past will be more encouraged to do so regularly in the future, and this should have a beneficial effect on the number of exhibitors.

SMC X-1 Observed at Energies > 7 keV

OBSERVATIONS of the binary X-ray source SMC X-1 are reported in next Monday's *Nature Physical Science* (April 23). These observations, made from the satellite OSO-7, extend to energies greater than 7 keV, thus complementing the Uhuru observations in the range 2 to 6 keV. The period found is consistent with the 3.8927 day period of the Uhuru data.

Ulmer *et al.* have also extended the known spectrum of SMC X-1, by means of the OSO-7 observations, to 35 keV (see diagram). The best fit to their data is a slope of $0.04E^{-1.24\pm0.09}$ photon cm^{-2} s^{-1} keV^{-1}, which agrees well with the rocket data of Price *et al. (Astrophys. J. Letters,* **168,** L7 ; 1971) which were obtained in 1970. The integrated luminosity from 7 to 35 keV is 4.5×10^{38} erg s^{-1}, assuming a distance of 63 Mpc, and there is evidence, say Ulmer *et al.,* that the spectrum steepens between 35 and 60 keV.
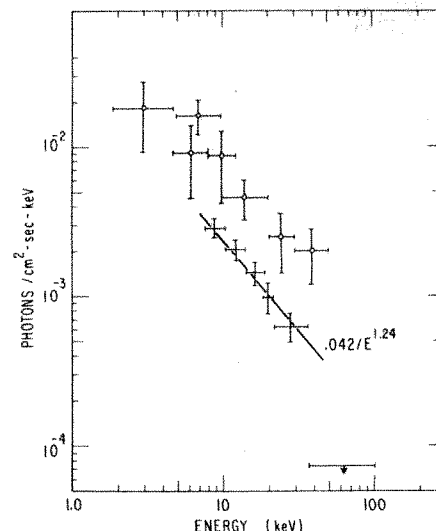
Spectrum of SMC X-1. +, OSO-7 observations reported in next Monday's *Nature Physical Science;* ○, rocket observations made in September 1970 (see text).

CHEMICAL SOCIETY

Pollution and Resources Discussed at Swansea

from Correspondents

BETWEEN March 26 and 30 the Chemical Society held its annual congress in Swansea. Two of the symposia were particularly topical, for they dealt with environmental pollution analysis and the winning of metals from lower grade sources.

Atmospheric Pollution

At the well attended meeting of the Analytical Division, participants listened to and discussed ten contributions which were chiefly concerned with atmospheric pollution. The scene for the details of scientific procedure and instrumentation was set by a particularly fine keynote paper by Dr L. A. Clarenburg (Rotterdam Public Health Department). Hinting that analytical methods were already fairly satisfactory for most pollutants and that the search for new ones had a low priority, he stressed the real environmental problem of building them into an integrated regional industrial system for what he termed "real-time" analyses to study the progressive build-up of potential pollution incidents.

Quoting the example of the Dutch experiments at Rijnmond and Vlaardingen, Dr Clarenburg showed how problems of odour in the former and SO_2 in the latter had been studied against the natural environmental parameters of time of year and day, temperature, humidity, wind speed, light intensity, natural particulate levels and so on. In both instances continuous monitoring signals from strategically sited automatic sensors were fed into a central computer. This machine was programmed to assess the data against the natural parameters and produce an early warning of potential incidents in sufficient time to allow the industrial concerns in the area to moderate or, if necessary, shut down their appropriate activities, thus minimizing the buildup of the symptoms and preventing further progression of the potential incident. Some particularly interesting points were raised, for example, the synergistic effects of multiple odours and environmental parameters, the supersensitivity of the human nose and the psychological as opposed to the physiological aspects of smell. (His recent report in *Zeitschrift für Analytische Chemie*, **263**, 198 ; 1973 merits reading).

In a fascinating contribution on pollution studies of the upper atmosphere, using Concorde 002 as the flying "laboratory bench" and submillimetre interferometric spectrometry as the technique, Dr N. W. B. Stone (National Physical Laboratory, Teddington) discussed the potential "pollution" of the stratosphere by water vapour from trans-sonic jet aircraft. What effect would the injection of considerable amounts of water vapour into the lower and intermediate layers of the stratosphere have? What are the present levels? Had they been seriously influenced already by military supersonic aircraft? Would the injection of hydrocarbons, nitrogen oxides and so on from jet engines seriously upset the photoionization balance? A sensitive technique seems to be available here for the study of the natural levels before trans-sonic flights can directly disturb the situation.

Multiple analyses of atmospheric levels of ozone, hydrocarbons, sulphur dioxide, carbon monoxide, nitrogen oxides and so on by gas liquid chromatography using flame ionization and chemiluminescence detector systems in an automated apparatus were described by Dr R. G. Derwent (Warren Spring Laboratory, Stevenage). In the study of traffic pollutants he finds that procedures made selective by adsorption stages inevitably lead to loss of detailed information, whereas those based on properties, such as chemiluminescence of gas phase reactions, are usually selective, sensitive and fast responding; for example,

$$NO + O_3 \rightarrow NO_2^* + O_2$$
$$NO_2^* \rightarrow NO_2 + h\nu$$
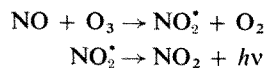
Much interest was evoked by Dr Derwent's description of the 0.132 p.p.m. of ozone found in the atmosphere of London by this technique. This is slightly above the upper "safe" limit of 0.1 p.p.m. The lachrymatory effect of ozone is felt at 0.2 p.p.m. and the "safe" concentration of 0.1 p.p.m. is based on an exposure for 1 h. Little is known of the effects of longer exposure to lower concentrations, but it might be significant that in Los Angeles, where more abundant sunshine could lead to longer exposure to ozone, the limit has been set at 0.08 p.p.m.

The three contributions mentioned here were typical of the other seven. Less attention was, however, paid to water pollution, but the keynote paper from Dr A. C. Docherty (ICI Agricultural Division, Billingham) more than redressed this in its quality.

Chemistry and Metallurgy

When the late Sir Ronald Nyholm proposed the symposium on metals from lower grade sources he felt that it would bring together chemists and metallurgists to discuss problems to which each could contribute. Furthermore, it would demonstrate the interdisciplinary nature of much of modern science and technology, particularly in its applied aspects. The result provided good fare for substantial audiences by no means confined to those professionally involved.

Apart from the question of funding the massive, high-risk cost of modern large-scale mining and metallurgical operations, the chief problems facing the industry are similar to those of the chemical process industry, namely, exploration and depletion of reserves; the environmental impact of large-scale mining and metallurgical processing, including the problem of the emission of SO_2; and the accurate technico-economic appreciation of new process technology as compared with existing technology. In the production of non-ferrous metals, environmental pressures have greatly accelerated the rate of commercialization of the newer pyrometallurgical processes, and interesting controversy continues on the possible future scope of hydrometallurgical techniques combined with solvent extraction and/or electrolysis. A little further into the future, the possible impact of chlorination technology arouses keen discussion.

Growth and Reserves

Metal usage is an essential feature of industrial society and Dr A. J. Robinson (Warren Spring Laboratory) pointed out that consumption of most metals doubles every 16 to 20 years, with aluminium and copper much above the average. The resultant large scale of mining and metallurgical operations has been one of the principal factors in maintaining real prices below those of 60 years ago. Drs B. G. Baldwin and D. Christie (British Steel Corporation) pointed out that an iron blast furnace producing 1,000 tons a day would have been considered normal in the 1930s, but daily outputs of 7,500 tons are not uncommon in Japan today and predictions for the 1980s run as high as 16,000 tons a day. Their contribution emphasized the value of accurate models of iron blast furnace performance to the complex problems, among others, of furnace burden preparation and the ore purchasing policy of the British Steel Corporation. Unlike some non-ferrous ores, plentiful supplies of rich iron ore remain available but they are distant and present logistic problems, and their scale of usage and relatively low cost leaves little margin for technical error.

Copper ores are trending sharply downwards in grade, but Mr M. J. Cahalan (Rio Tinto-Zinc) pointed out that proven reserves at current prices have kept pace with demand; he also noted that the high cost of exploration deters the extension of proven reserves beyond 50 years. In working leaner ores, Dr Robinson indicated some of the advances that have been necessary in selective flotation since it was first commercialized in Australia in 1909, in

milling and materials handling, and in the highly sophisticated methods of analytical control now in use.

Although flotation research continues to be active, Dr Robinson thinks that specific flocculants to deal with particles of 1–20 μm might become important. These techniques, and improved large-scale mining methods, are making possible the economic working of lower grade ore bodies and Dr D. Slater (Institute of Geological Sciences) reviewed mining possibilities in Britain from the geological standpoint, mentioning some of the newer analytical and theoretical techniques which are being brought to bear on the problem. Copper, tin and possibly nickel seemed to be the likeliest possibilities, but it seems unlikely that the recently developed Irish lead–zinc deposits extend across the Irish Sea. Dr T. W. Farthing (Wolverhampton Metal Holdings) gave a fascinating account of the economics and technology of the secondary and scrap recovery industries, but he pointed out that the highly fragmented structure of the collection part of the industry militates against the kind of technological improvement recently made on the more integrated refining side.

Process Technology

Process technology has evolved rapidly during the past 20 years and Professors F. D. Richardson (Imperial College) and P. A. Young (University of Leeds) presented some aspects of their physio-chemical investigations typical of those necessary as a foundation for advance. Professor Young and others showed the recurrent importance of accurate phase diagrams for the interpretation of the behaviour of slag systems. Over the whole range of metals, pyrometallurgical smelting continues to predominate with the newer processes offering solutions to the problem of SO_2 emission, which is inseparable from the smelting of sulphide concentrates. Dr Robinson and Mr Cahalan reviewed newer copper processes, including the Outokumpu flash smelting process, the Kaldo rotary converter and continuous processes of the Worcra, Mitsubishi and Noranda types, and analysed conditions for disposal of sulphur as sulphuric acid or, potentially, as elemental sulphur. Mr C. F. Harris reviewed the Imperial Smelting lead–zinc blast furnace, emphasizing particularly its complementary rôle to Waelz treatment and slag fuming in the treatment of low grade and complex materials, and the environmentally acceptable nature of the slag produced by the furnace. Recently escalating coke prices are stimulating processes based on electrical energy for zinc and copper. Mrs Baldwin and Christie showed that this is not a dominant factor in iron production, but

the account by Drs J. B. Cartwright and G. B. M. Eastmond of electroslag refining illustrated how development is making this process applicable to lower alloy steels.

The combination of hydrometallurgical leaching with solvent extraction is attractive environmentally and Mr A. W. Fletcher (Warren Spring Laboratory) related how considerable research and development in this field is beginning to have an impact on copper processing, topics also discussed by Dr Robinson and Mr Cahalan. Mr Fletcher reviewed the "intense" Forward, Arbiter and Cymet ($FeCl_3$) processes, all of which utilize a leaching stage under rigorous conditions followed by solvent extraction. He also reviewed the future possibilities of biological leaching as a means of economically working low grade ores and dumps. Work on all of these processes is stimulated by the in-

creasingly stringent emission and effluent controls being placed on conventional smelters.

Chlorination offers many theoretical advantages for metal extraction and some of these were exemplified in the lucid review by Dr S. C. Townshend (International Nickel) of very recent laboratory studies on the hitherto intractable limonite nickel materials. A more general review of chloride processes was given by Mr D. V. Jackson (Warren Spring Laboratory), who pointed out that wider adoption of such technology had been hampered by construction problems with materials; adequate pilot-scale demonstration plants were particularly necessary to overcome fears and objections on this score. The outcome of Alcoa's new route to aluminium, based on $AlCl_3$, would be awaited with interest from this viewpoint.

Gravity Surveys in Scotland

ALTHOUGH the geology of the Tertiary intrusive complexes of Skye, Mull and Ardnamurchan (North-west Scotland) has received considerable attention for many decades, these bodies have, perhaps surprisingly, been subject to relatively little geophysical investigation. In next Monday's Nature Physical Science (April 23), however, this situation is remedied to some extent by Bott and Tuson who report the results and interpretations of gravity surveys carried out over all three complexes.

In all cases the Bouguer anomalies are positive, being particularly large over Skye and Mull, and thus indicate the presence of large underlying volumes of relatively dense igneous material. In the Skye intrusive complex almost equal surface areas are occupied by basic-ultrabasic and granitic plutonic rocks; but the Bouguer anomaly indicates a very different picture at depth. After subtraction of the estimated regional background, the maximum amplitude of the near-circular anomaly is +53 mGal. Because basic and ultrabasic igneous rocks are usually denser than the metamorphic basement, whereas granitic rocks are less dense, Bott and Tuson infer that at depth basic-ultrabasic igneous rocks predominate.

The principal density contrast giving rise to the positive anomaly over Skye must therefore be that between the basic-ultrabasic rocks and the gneissose basement. Looking at the situation in terms of a detailed model, Bott and Tuson conclude that the minimum possible contrast between complex and basement must be 0.18 g cm^{-3}. Although the precise density of the basic-ultrabasic body is not known, this implies that the overall density of the intrusive complex is greater than that (2.95 g cm^{-3}) of the average gabbro represented by surface

samples. Bott and Tuson thus assign a minimum density of 3.01 g cm^{-3} to the subsurface body which is taken to have a roughly rectangular plan and to widen gradually from the surface to the base at a depth of about 14 km.

By this interpretation the subsurface intrusive body has a volume of about 3,500 km^3 of which less than 5 per cent can be granite. Because no interpretation of gravity is unique, Bott and Tuson also offer a second model in which the non-granitic part of the intrusion has a density of 3.15 g cm^{-3}, the maximum depth is 5.5 km, and the widening with depth is more rapid than in the first model. In this case, the intrusive volume is about 1,500 km^3 of which granite forms about 7 per cent. Between these two extremes there is a whole range of models consistent with the Bouguer anomaly, but in no case can the volumetric proportion of the granite in the intrusion exceed about 8 per cent.

The surface geology of the Mull complex is quite different from that of Skye, granitic rocks being most abundant. Nevertheless, the Bouguer anomaly over Mull is similar in shape, area and amplitude to that over Skye, indicating a similar subsurface structure. Again, therefore, non-granitic rocks must predominate in the intrusive body. (In the case of Ardnamurchan the gravity is not well enough defined for a full interpretation to be possible.) As Bott and Tuson point out, the unexpectedly large volumes of basic-ultrabasic material beneath Skye and Mull make it more difficult to explain the origin of the intrusive complexes. Their own suggestion (which agrees with a previous one based on the geology alone) is that magma has risen from the lower crust by repeated stoping and/or cauldron subsidence.

Environmental Archaeology in the Western Negev

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The extent of change in environment and settlement during the past 1,500 years was demonstrated last year in the semi-arid zone of the western Negev by a multi-disciplinary British team.

IN recent years, European archaeology has witnessed the development of new methods of research, adding to the study of man's artefactual evidence a study of ancient environment, its ecology, climate, geomorphology and allied subjects. In Western Asia, long the home of great archaeological discoveries, this newer study has, however, been slow to develop. Frequently the scientist has been called on only as an adjunct to the older study, and his work published in appendices as a sop to the scientific world. The greater discipline now demanded within the subject calls for a more consolidated examination of areas in Western Asia so that the interpretation of the archaeological evidence may be placed on a more rational footing. The prime movers in this field of study in the Near East have been particularly Vita Finzi and Higgs[1] as well as Legge et al.[2].

In a further attempt to redress this balance, a survey was begun in Israel during the summer of 1972, the intention being to create a team of scientists whose interests also touched on the archaeology of the region; thus the team would comprise a botanist, chemist, geomorphologist and environmental specialist together with the archaeologist. The ancient environment would then be studied as a prerequisite to the study of man[3]. Such an interdisciplinary team would examine an area of marginal agriculture, where the environmental factors would be most critical, in order to set parameters on its modern and ancient environment, to study the present flora and to compare this with residual ancient pollens and charcoal from datable deposits, to follow the geomorphological history of the area in its construction and appearance in ancient times, to analyse its soils for chemical composition, particle size and history, and to focus these disciplines on archaeological sites in the area.

The area selected was the region around Tell Fara, in the Negev desert near Gaza. An isolated semi-arid region bisected by deep dry river beds, the Negev lies in the southern coastal plain of Israel, south of Tel Aviv and south-east of Gaza. There were two reasons for this choice. First, this is an area where normal agricultural methods produce an extremely precarious economy, balanced between scant success and abysmal failure. Thus minor fluctuations can have far-reaching consequences in settlement patterns and land use. Second, it has been known in the past as an area rich in archaeological material, dominated as it is by a typical Bronze Age/Iron Age site[4] (Tell Fara) from 1800 BC to the Roman period. In the surrounding areas, pre-urban settlements have been discovered which date from the fourth millenium BC. Previous excavators

have also believed that even earlier material from the Palaeolithic period (stretching back many millenia before 12,000 BC) is present. A correlation of these deposits, if located, might well offer suitable dating criteria for the environmental research.

Geology

The results are preliminary, but already vindicate the theory. Geologically, the lowest rocks in the area are a series of fossil dunes forming a series of headlands on which the tell itself stands. In part these dunes are overlaid by a bed of heavy gravels, some of the larger cobbles of which show signs of marine battering. Both of these strata are partially covered by a very heavy deposit of loess, the uppermost layers of which now form the country surface of the western Negev. Erosionally the area is dominated by the Wadi Ghuzzeh (Nahal Basor), a situation which can be proved to have existed for at least the past 50,000 yr as it is seen to be bounded by ancient sites. At present the level of the wadi is on the gravel, well below the loess strata.

In winter, the wadi is fed from several deep gullies extending back into the relatively soft loess and dissecting the country surface thus creating an extensive area of "badlands". The morphology of this area is extremely complex, with much redeposition of material. In general, however, there is a history of an underlying system of erosion and deposition of the loess during the past 50,000 yr which has produced a series of roughly horizontal layers to a total depth of some 30 m. Several of

Fig. 1 Area around Tell Fara, Israel. In the right middle ground are the soundings of the Levalloiso/Mousterian floor, beneath some 30 m of loess.

Fig. 2 Tell Fara (left foreground). Left distance, fossil dunes; centre Wadi Ghuzzeh; right distance, loess badlands. Note the large stands of young tamarisk in the wadi.

these strata are heavily oxidized and weathered bands, indicating periods of arrested deposition, but superficially at least these bands are very similar in texture and appearance to the seasonally arid, weathered, tropical soils. (For a discussion of palaeosols on this area see Dan and Yallon[5].) A stratigraphic column of these deposits was traced and samples collected which should provide at least a relative sequence of soil data for the evaluation of the changing face of the Negev.

Botany

As no exhaustive collection of plant material is available in Britain, as complete a collection as possible was made of the present summer flora, which amounted to the striking number of 107 species. In spite of the obvious lacuna in spring annuals, the figure was higher than expected. These were pressed in the field, their fruits were pickled and their seeds collected. Secondary wood from trees in the wood was sampled. The classification of the plants is now complete and thus forms both a reference collection for comparison with ancient plant evidence and a control on the modern environment.

The plants appeared in very marked zones, some of which ran parallel to the water course and some at right angles to it. The obvious explanation of the former is water availability, but for the latter a different solution must be found, possibly a combination of the mechanical and chemical composition of the soil.

Two trees were noticed, *Acacia raddiana* and *Tamarix nilotica*. These two have frequently been recorded in this part of the Negev[6]. In the area surveyed, however, only one mature specimen of acacia was found, and only two or three old tamarisk. On the other hand, thousands of saplings of acacia testified its natural position in the area, and large stands of young tamarisk dominated the wadi floor. Clearly this new growth indicates some fairly recent change in the area.

Archaeology

Several sites were located and investigated, two of which provided the necessary termini for the geomorphological column. Near the base of the loess were several sites dating from the Middle Palaeolithic (Levalloiso/Mousterian) period, at least one of which was an undisturbed deposit with bone

and charcoal appearing in equal quantity with the flint tools. From these sites a picture can be built up of the pre-agricultural Negev, its surface and appearance. Doubtless these sites are concentrated on an ancient water hole, for copious faunal remains of primitive cattle (*Bos*) and large red deer (*Cervus* (?) *elaphus*) occurring in the deposit show it to be an open butchering site. Analysis of the charcoal *in situ* and of the pollen now found to be present in the stratigraphic column will render an approximation of the contemporary flora. This site then and its data give a lower terminus to the survey of about 50,000 BP.

At the other extreme, on the top of the present country surface were the remains of a Byzantine farmstead, once a prosperous settlement, its buildings, cisterns and fields now almost completely eroded away. Pottery from the site dates it as the period of Justinian, around 550 AD. The walls of the buildings had been undermined by erosion and now lay collapsed in the resulting gullies. The silt dams constructed across the ravines below to collect the eroded soil each year and thus snatching a harvest from the low rainfall have long since been breached. Only a once-subterranean cistern, now standing above ground level, remains intact. Clearly, although the pre-Byzantine period may have been one of deposition, the post-Byzantine period was one of fierce erosion. It will be in the period between 50,000 yr and 2,000 yr ago that environmental evidence will have the most significant archaeological application. The necessary laboratory work involves the extraction and determination of pollen from the samples covering this period. Difficulties arose in the extraction of pollen from loess deposits, but these have now been overcome by the application of flotation techniques[7] and ancient pollen is being recovered. The programme of soil analysis must also be completed before any interpretation is attempted. On the other hand, the past 1,500 yr may be used as a model for the type of results that one might hope to obtain. During this past one and a half millenia three environmental periods can be distinguished in the area.

Three Periods

The remains of the Byzantine farmstead show that in its day it covered an extensive area of some 5,000 m² of buildings. Its farmed land probably extended beyond the use of silt dams

to the cultivation of the country surface. This was the last phase of the heyday of Negev agriculture. Either through economic pressure, or more probably political necessity, this style of agriculture died out following the Omayid invasion of the mid-seventh century, never to be repeated. It was at this time that the Bedouin, no doubt always present in the fringes of these previously semi-urban areas, were drawn into the vacuum. These Bedouin are not the camel nomads of the East, but semi-nomadic roving pastoralists, living from their herds of sheep and goats, and from scant farming. The natural result of this type of exploitation was overgrazing and denudation of trees with consequent floral deterioration and soil erosion[8]. Evidence of this new erosional phase is to be seen in the almost total annihilation of the Byzantine buildings by a dendritic system of gullies which has eaten back into the country surface during this time.

The arid position thus promoted has persisted in the area until very recently. Photographs taken of the area during the 1920s and 1930s show a treeless, parched landscape[4]; but now the area has changed to a ground cover which even in summer can be lush. Because the Israeli government has embarked on a resettlement plan for the Bedouin during the past few years, they have been discouraged from using the area. As a result, the new natural growth is dramatic, hence the large stands of immature acacia and young tamarisk that have

recently begun to dominate the area once more. Although the flora can never return accurately to its pre-occupational ecology, there is a tendency for natural flora to recur at this time.

This model has illustrated the extent of change in environment and settlement over the past 1,500 yr, which would itself result in archaeologically significant alterations. To quantify these interdependent factors for earlier periods will require more research in the area, and to this end a further season is planned for 1973.

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Algeria's Answer to a Manpower Problem

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Algeria is combating a severe shortage of skilled people by means of technological institutes geared closely to the nation's manpower requirements.

ALGERIA'S biggest problem on gaining independence in 1962 was the severe shortage of skilled manpower caused by the European exodus. High priority was given to the expansion of education to create a class capable of doing both the jobs previously done by Europeans and also the new administrative and technical jobs which the demand for development created. Between 1963 and 1969 the number of children in primary education doubled—the percentage of children in primary schools was raised from 25% in 1962 to 53.71% in 1970—and the most realistic forecasts aim at achieving universal primary education in the early 1980s. Expansion in secondary education has been even more rapid: between 1963 and 1969 the number attending quadrupled. The overall figures for university expansion too are impressive: between 1963 and 1969 the numbers increased ten-fold.

This massive expansion could only have been carried out with massive investment. In 1970 Algeria devoted 23% of the national budget to education and under the Four Year Plan (1970–1973) 11% of the total investment is for education and training.

But these overall figures conceal an alarming wastage rate. Only 54% of the children entering primary schools

complete their primary studies, and, of these, about 20% go to secondary schools; only 15% of children entering secondary schools complete the 7 years. Wastage at university level is also high; only 10% complete their course. The authorities are obviously concerned by this wastage and the great investment that shows so little return. In some fields the situation has even worsened. Rather than encouraging their children to become technicians or skilled workers, many parents prefer to send them on a fruitless chase after more "respectable" paper qualifications, leading frequently to unemployment. The educational system does not produce the kind of manpower which the economy needs.

The new needs engendered by the Four Year Plan and the replacement of foreign personnel by nationals are enormous. Algeria has engaged in an ambitious plan of development whose success depends on a considerable increase in the number of technicians, scientists and administrators, and yet is unable at the moment to meet even the demands of the present. The demand for advanced training in engineering (21,000) is three times greater than existing educational facilities could satisfy (7,000). Whatever progress education has achieved it is completely out of tune with economic reality. The real problems of development cannot be solved by the mindless expansion of a system that had been designed to meet the needs of a French colony. An initial phase of educational expansion should give way to an educational system tailored to the economy, culture and social needs of Algeria. A National Commission for Educational Reform was set up, but its proposals will not be implemented before the end of the period

of the Four Year Plan. Trained manpower requirements, however, must be met within this period. Drastic change in institutions, methods, contents and priorities was therefore vital and a short cut had to be taken.

Setting up Institutes

Alongside the existing educational system a new training system has been set up to provide, within the shortest possible time, those specialists most urgently needed for Algeria's development.

In 1970, the Institutes of Technology were opened in response to these needs. They are to offer training on a large scale based both quantitatively (through the calculation of numbers required at different levels of skills) and qualitatively (through the adaptation of content and methods of specific requirements) on manpower needs. The institutes are thus to train 17,710 people at an intermediate level and 9,930 at a higher level for the industrial sector, and 55,200 skilled workers and people at an intermediate level and 15,910 people at a higher level for the social sector, within the period of the Four Year Plan.

Such a system will only be temporary; the reformed school system should eventually take over its functions and the institutes will then become in-service training centres or will provide refresher courses for those already employed.

Accordingly, no investment was made in building and equipment; instead existing facilities like vacant premises, buildings not utilized to their fullest extent, and disused army barracks were called into play as much as possible. Only DA 200 million (£17 million) was allocated to the institutes for capital expenditure whereas DA 2,718 million (£230 million) went to the national education sector.

As the training provided must be adjusted to manpower demand, job analysis studies are used to define the tasks; from these can be obtained details of responsibilities, skills and personal qualities required for a particular occupation. These observations are then translated into training objectives and syllabuses. The learning process follows the principles of on-the-job training; practical work and an outside assignment form an integral part of the course and field-work underlies theory.

Recruitment is not based on a diploma, but on the applicant's general educational level, and on his motivation, aptitudes and desire to work; students are mostly secondary school drop-outs who, until now, have found it almost impossible to find themselves a niche.

The project was not seriously examined until 1969 when a commission was set up; this included representatives of all the ministries involved, of administrative and business concerns and of educational organizations. Eight project chiefs to be responsible for all the preliminary work involved in the actual launching of these institutes were appointed. Seventeen categories of institute were provided for: the Institutes of Agriculture (engineers; one), Agriculture (technicians; seven), Chemistry (one), Commerce (one), National Education (twenty-one), Electromechanical Maintenance (one), Finance and Accounting (one), Hotel and Tourism Trade (one), Hotel Trade (one), Agricultural and Food Industries (one), Metallurgy and Mining (five), Planning Techniques (one), Public Health (three), Telecommunications and Electronics (one), Public Buildings and Works (one), Topography (one) and Youth Services (under study).

Administering the Institutes

The first institute launched was the Mostaganem Technological Institute of Agriculture; it was opened in January 1970. It provides training for higher level engineers and specialists for the agricultural sector. Since then thirty-three others have been set up, including twenty-one Ecoles Normales which have been converted into Teacher Training Institutes.

The managing body of each institute is the Administrative Council; one of its chief functions is to consider job placement of graduate students. Its members include, among others, representatives of the prospective employers: the "users"—the involvement of the users in the planning and running of these institutes is one of their distinctive features. This makes sure that the training provided meets the needs and will also ensure a balance of supply and demand on the labour market.

All the directors of these institutes are Algerian and higher education graduates. The teachers are either teachers from traditional schools, specialists from enterprises who work part-time in the institutes, or foreigners recruited under technical assistance agreements. The
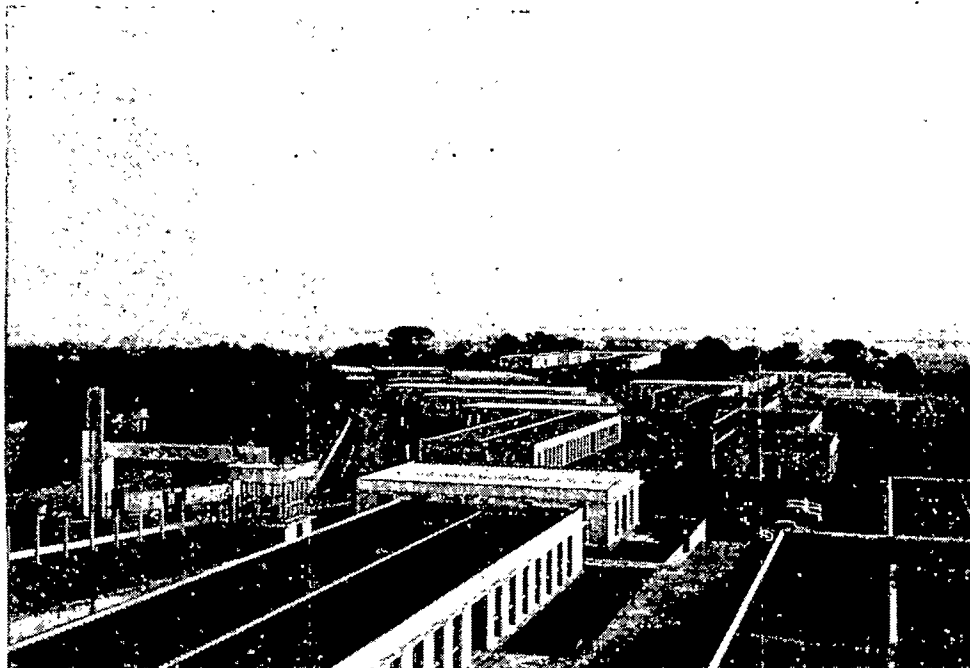
Fig. 1 The Ben Aknoun complex in Algiers. This houses three institutes—the Technological Institute of Commerce, the Technological Institute of Finance and Accounting and the Institute of Planning Techniques.

students work in small groups and the staff-student ratio is one to ten. Approximately 1,500 teachers are employed at present.

As the student is trained for a specific job he is more or less considered as an employee: he receives a training allowance and benefits from the same social security scheme as salaried personnel in public service. Furthermore, contracts are entered into by the institutes or the student, on the one hand, and the enterprise or public service on the other, to guarantee employment to the student trainees on completion of training. The graduate trainees are, however, required to work in the service of the enterprise to which they have been appointed for a period corresponding to the length of training.

Achievements

Looking at what has been achieved after a year or so of existence, it is clear that, in spite of all the difficulties encountered, and the setbacks and delays, the implementation of the programme is well advanced and a considerable amount of experience has been gained.

Of the candidates who applied following a publicity campaign in the summer of 1969, 18,305 were selected on the basis that they had at least reached the standard of a fourth form in a secondary school, that they were not employed and were not enrolled in a school. Their general and specific attitudes were tested; then during the summer of 1970 a two month course was organized. After this course tests were given and their results used for selection of the students to be admitted to the institutes the following September.

There are at present more than 13,000 trainees on courses at these institutes, including 7,692 technicians, 4,385 engineers and cadres and 1,182 qualified workers. Of the applicants who attended the preliminary course during the summer of 1970, it seems that 92% of the boys were under 22 (69% under 20), whereas 96% of the girls (who represent only 9% of the whole group) were under 22 (79% being under 20). The proportion of younger students is likely to increase as the scheme is more fully implemented. The launching of several institutes has had to be postponed because of administrative difficulties or delays suffered in the construction or the conversion of buildings. These delays are mostly a consequence of the shortage in qualified personnel in the ministries to carry out the necessary manpower surveys, translate this information into training objectives, determine the length of training, decide on the appropriate methods of teaching and on the syllabus, and so on.

Successes and Difficulties

If it is possible, after nearly two years of existence, to take stock of the numbers of institutes opened and the numbers enrolled, it is too early yet to assess the achievements qualitatively. As the purpose of these institutes is to train personnel who will be directly adjusted to a particular job, it will not be possible to assess the overall value of the training provided until these trainees are engaged in production. A number of positive aspects can already be stressed nonetheless: periods of integrated practical training have been organized and have been welcomed by the public services or concerns, study trips have been conducted throughout Algeria; and formal lectures have been replaced by work in small groups. Most of the trainees readily accepted the methods of active education. A number of difficulties have, however, been encountered as regards self-assessment and self-discipline, and there is less satisfaction with the results of those converted institutions where the project is run on more traditional lines.

The principal difficulties have arisen from the "diploma"

issue; also the rules governing the students within the Civil Service, after they have completed their training, have not turned out to be easy to define.

Great difficulties have also been encountered as regards credits and the recruitment of staff. It was impossible to find locally a sufficient number of qualified teachers and it was therefore necessary to rely heavily on foreign assistance. In the long run the most important problem will be the training of local instructors to replace the non-Algerians. Several institutes have made provisions to draw instructors from among their old students, and we would also like priority to be given to the institutes when university students are appointed to the public services for their two years of national service, during which they are obliged to do a job assigned to them within their speciality.

There have been criticisms of costs and charges of excessive specialization. Costs are certainly very high, but it has not yet been possible to carry out an analysis of the cost per student trained. One must, however, bear in mind that these students will be operational as soon as they have completed their training, for the training has been based on a systematic analysis of the job concerned in close cooperation with the users: this should reduce wastage and therefore diminish the cost.

The other criticism relates to excessive specialization. Narrow specialization is a necessity if Algeria really wants to fill the shortage in qualified manpower and wants its industry to take off. A more general academic form of education would place too much emphasis on the individual as such and not enough on the productive worker: there is need for technical education related to the performance of a job: this is the first priority and it is only an exceptional response to exceptional circumstances. With the eventual return to a normal situation, the institutes will no longer have to maintain such a fast rhythm and will provide further training and retraining of those already employed. The vocational training which they offer will also be supplemented by programmes of general educational value produced by the National Centre for Generalized Education through radio, television, the press and correspondence courses.

The Institutes of Technology are an educational experiment which cannot be developed in a void; they must be firmly rooted in the life directly around them. They must contribute to improving the standard of work and life in their areas, and to the building up of a socialist society. In fact, they are already beginning to do this and the Mostaganem Institute of Agriculture, for instance, has already organized numerous periods of field work in agricultural estates under workers' management. Also the fact that the graduate trainees are bound under a contract to work in the service of the enterprise to which they have been appointed for a given period will help to shift the focus of development away from the urban areas to the rural or poorer areas.

The Algerian experiment might well be of interest to other countries in the Third World where the same problems need to be tackled: problems like school drop-outs or even school-leavers holding diplomas and flocking to the cities but unable to find employment, most of them being functionally useless because they come from a non-functional educational background. At the same time, there is an acute shortage of the skilled manpower, especially of intermediate level, required to supply the needs of the economy and to break out of underdevelopment.

Our ambition is thus not only to train sufficient numbers of personnel of sufficient quality to meet the needs of the economy, to innovate in teaching methods and programme contents and give further opportunity to those denied it, but also, if we achieve these aims, to serve as a creative model for other developing countries which have the same problems.

Ground-based Measurement of Millimetre-wavelength Emission by Upper Stratospheric O_2

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Measurements from ground level of 53 GHz radiation from molecular oxygen in the stratosphere, using a very precise radiometer, can be used to give stratospheric temperatures.

THIS article reports measurements at sea level of upper stratospheric thermal emission from five high-rotational, millimetre-wavelength, magnetic dipole transitions of molecular oxygen, and discusses use of the emission lines for remote sensing of upper stratospheric temperatures. One of the lines, the 27_-,

Molecular oxygen has a band of spectral lines near 60 GHz (5 mm wavelength) and a single line at 118 GHz produced by changes in orientation of its electronic spin relative to its rotation. The individual spin-rotation lines are designated N_+ or N_-, where N is the rotation quantum number which must be odd for $^{16}O_2$ in the $^3\Sigma_g^-$ electronic ground state, and where the subscript indicates whether the change in total angular momentum of the molecule during an emission transition is $+1$ or -1. Each $N_\pm$ line has $3(2N\pm1)$ Zeeman components spread over $\sim \pm 1$ MHz by the terrestrial magnetic field. Near the centre of the 60 GHz band the terrestrial atmosphere is quite opaque, but on the band edges thermal emission, originating in the upper stratosphere where the lines are relatively narrow, can penetrate the lower atmosphere and can be measured at the ground.

Fig. 1 Measured (upper) and calculated (lower) atmospheric zenith emission. Each measured line and the instrumental baseline shown beneath it represent integration for 16 min. The measurements were made during the week of August 30, 1972.
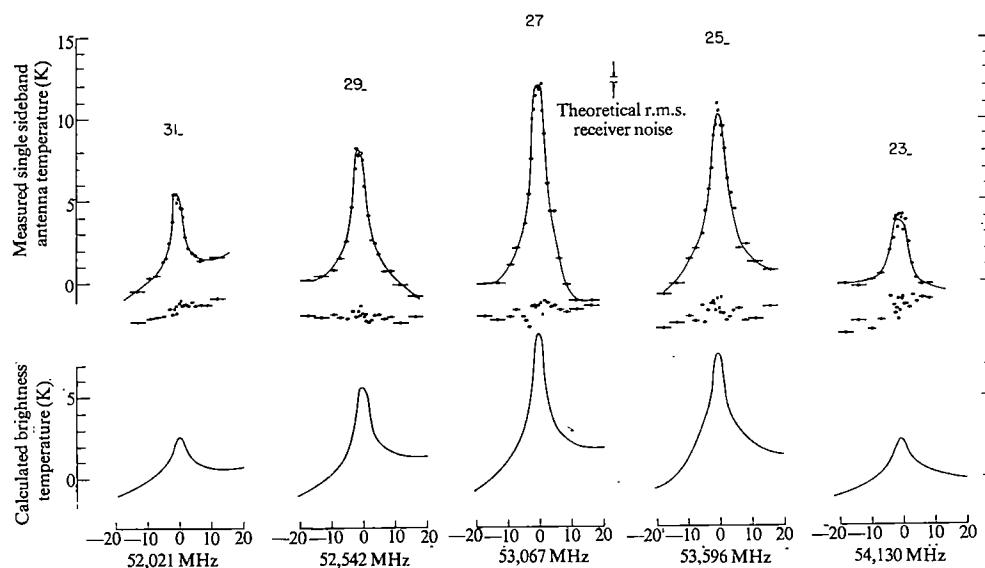
has been reported earlier in solar absorption[1] and in emission[2] but with poorer signal-to-noise and frequency-resolution than the measurements given here, and wings of some of the lines are evident in previous aircraft absorption measurements[3]. Stratospheric emission lines of submillimetre wavelength have also been observed recently from aircraft by a different technique[4,5].

The measurements reported here were made during very clear sky conditions at Haystack Observatory (elevation 0.15 km) in Westford, Massachusetts, with a radiometer constructed at the Massachusetts Institute of Technology[6]. The radiometer was a load-switched superheterodyne microwave receiver with a noise temperature of 1,800 K and no rejection of the image sideband. A linearly polarized standard-

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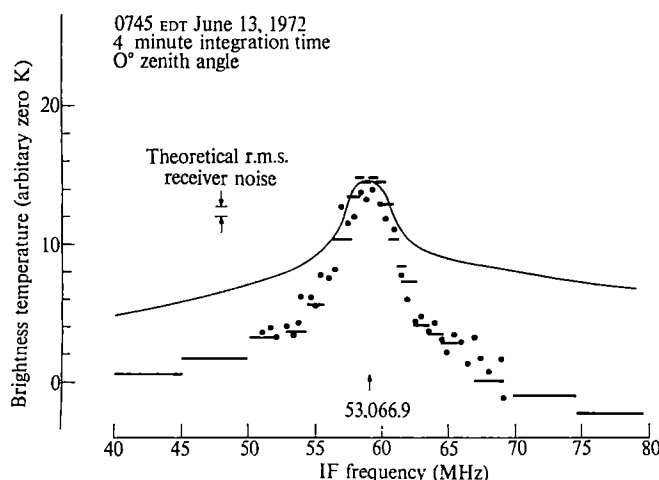
Fig. 2 Measured and calculated zenith emission from the 27_ line. The zero levels of the measured and calculated lines are adjusted to give agreement at line centre. ▬, Filter system measurements; ●, haystack correlator measurements; ——, calculated for 1962 US standard atmosphere.

gain microwave horn (10° beamwidth) was the antenna. The local oscillator, a klystron phase locked to a crystal reference, had frequency stability and absolute accuracy of 10^{-2} MHz. Spectral analysis was performed both by a twenty-three-channel filter bank and by the 100-channel Haystack digital autocorrelator[7]. The filter bank covered a total bandwidth of 40 MHz, with individual filters having resolutions ranging from 0.5 MHz for the centre channels to 5.0 MHz for the outer channels. Two bandwidths were used with the autocorrelator: 20 MHz with 0.5 MHz resolution, and 6.67 MHz with 0.16 MHz resolution. A small digital computer processed data from the filter bank. Data from the autocorrelator were Fourier-transformed and further processed by the Haystack computer.

Table 1 Centre Frequencies, ν_0, and Base (−20 MHz from the Line Centre) Absolute Zenith Brightness Temperatures, T_B, for the Oxygen Lines

Tran-sition	Measured ν_0 (MHz)	τ (nepers)	T_B (K)	T_B, including image sideband (K)	Measured T_B, including image sideband (K)
			Calculated (−20 MHz from line centre)		
23_	54,130.2±0.5	3.30	269	267	265± 2 (U)
25_	53,595.9±0.2	2.03	241	242	240± 5 (L)
27_	53,066.9±0.2	1.27	198	194	206±10 (U)
29_	52,542.4±0.2	0.88	161	163	174±12 (L)
31_	52,021.4±0.5	0.64	129	131	139±15 (L)

Uncertainties in the frequencies are attributable to the uncertainties in fitting the measured emission to the calculated emission; frequencies for the 25_, 27_ and 29_ lines are more accurate because they were observed with 0.16 MHz autocorrelation resolution. Uncertainties in measured absolute temperatures are attributable to the 10% calibration uncertainty. Beside the measured base temperature is indicated whether the line was observed in the upper (U) or lower (L) sideband. The zenith opacity τ calculated for the base of the lines is also given.

Figs. 1–3 show, with an increasingly expanded frequency scale, the measurements and the results of calculations. The intensities of the lines increase with frequency up to the 27_ line because the lower rotational states have larger populations, but decrease with frequency above the 27_ because of increasing attenuation by the lower atmosphere. A similar set of N_+ lines exists on the high-frequency band edge. The linewidths

of the measured emission correspond to pressures less than 10 mbar, proving that the emission originated at altitudes above 30 km. Table 1 gives the measured line frequencies, which agree to within measurement accuracy with the calculated values[8] (see also refs. 9 and 10). For each line, the local oscillator frequency was shifted slightly in a separate measurement to make certain in which sideband the line appeared. The vertical axis of each figure is the brightness (equivalent blackbody radiation) temperature of the emission. Absolute accuracy of the measured amplitudes is 10% as determined by calibration of the radiometer with liquid nitrogen and thermal loads, and zero levels in the figures are arbitrary; Table 1 gives absolute values for measurements and calculations. Instrumental baselines, measured at each observed line frequency by tipping the radiometer so the horn antenna was pointed at or below the horizon, where no spectral feature is expected, are shown beneath the measured lines in Fig. 1. Fig. 2 indicates the excellent agreement between spectral analysis by the filter bank and the autocorrelator. The high-frequency resolution measurement shown in Fig. 3 represents equal observation times with the observed electric vector respectively parallel and perpendicular to the Earth's magnetic field. As expected for the latitude of the measurement, no polarization was observed.
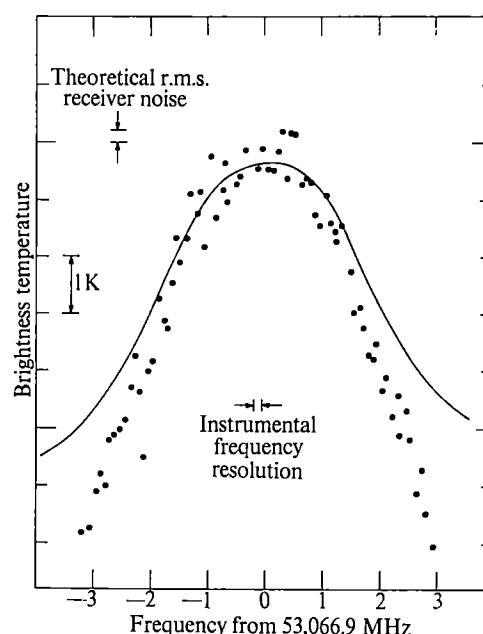
Fig. 3 High-resolution measurement and calculation of zenith emission from the 27_ line. The measurement was made 0200–0600 EST, August 30, 1972. ●, Measured; ——, calculated.

Calculations of millimetre wavelength absorption by O_2, first performed by Van Vleck[11], have been presented by several workers (refs. 12–17 and unpublished work of H. J. Liebe and W. M. Welch for the AGARD electromagnetic wave propagation panel). Zeeman splitting of the spin-rotation lines must be accounted for above ~45 km in the terrestrial atmosphere, where collisional broadening is sufficiently small that it does not mask the splitting. Lenoir[12] developed expressions to describe the polarized and anisotropic emission from the Zeeman components in the presence of a magnetic field and calculated emission from the mesosphere as seen from above. The calculations done here use Lenoir's matrix radiative transfer equations with the 1962 US Standard Atmosphere model[18], a magnetic latitude of 55° (at which the measurements were made), and a vector dipole model of the Earth's magnetic field[18]. Techniques used in the calculations

are described elsewhere[19]. A volume mixing ratio of 0.21 is assumed for O_2 and integrations are carried to 90 km. The Gross[20], or Zhevakin-Naumov[14], line shape is used with linewidth equal to the geometrical sum of Doppler[12] and collision[17] widths. "Zero frequency", $\Delta J=0$, O_2 transitions[11] are included by adding their absorption to the diagonal elements of the absorption coefficient matrix. Absorption by atmospheric water vapour and other minor constituents is thought negligible (~ 0.05 neper) and is not included in the calculations.
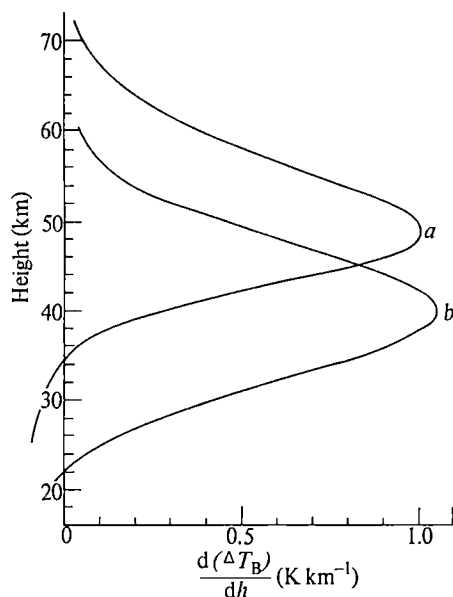
Fig. 4 Height resolution for ground-based sensing of upper stratospheric temperatures from O_2 millimetre-wavelength emission. a, $\nu_2 = \nu_0 = 53,066.9$ MHz; $\nu_1 = \nu_0 - 2.5$ MHz; b, $\nu_2 = \nu_0 - 2.5$ MHz, $\nu_1 = \nu_0 - 20$ MHz.

The discrepancy between measured and calculated line amplitudes is significantly larger than the radiometer calibration uncertainty. The image sideband contributes a slope to the measured lines, but cannot account for the amplitude disagreement. Atmospheric temperatures must be warmer than the model used for calculations by ~ 50 K at altitudes of 30–60 km in order to explain the discrepancy, a highly unlikely situation for the time and location of the measurements[21], and reported anomalous O_2 concentrations[22] occur at altitudes too high to contribute significantly to the emission measured here. The discrepancy probably arises from the theory used for the calculations, which sums the (assumed incoherent) absorption of the individual lines. A theory which accounts for coherence in overlapping lines has been applied[23] to absorption by pure O_2 at a pressure of several atmospheres and gives better agreement with measurement than calculations which simply sum individual line absorption. This theory has also been used[24] to calculate O_2 absorption at atmospheric pressures, but quantitative comparisons with measurement have not yet been made.

Previous publications have described how millimetre-wavelength O_2 emission can be used to sense temperatures up through the mesosphere from satellite-based measurements[12,13,16,27] and tropospheric temperatures from ground-based measurements[25-27]. Temperatures in the stratosphere can also be sensed from ground-based measurements of the O_2 emission lines reported here. High altitude emission is distinguishable from low altitude emission because of the strong dependence of linewidth on altitude up to ~ 50 km where Zeeman splitting produces an effective linewidth that is only a weak function of altitude. Emission above ~ 70 km

contributes negligibly to the lines because the absorption coefficient at line centre is then proportional to O_2 density, not to mixing ratio as when collisions dominate line broadening, and line emission decreases exponentially with altitude. Variations in absorption by the lower atmosphere can be corrected for by measurements of the base of the line. Fig. 4 shows the altitude region sensed by the ground-based measurements, where the two curves give as a function of altitude the contribution per unit altitude to the measured emission at the ground. The curve with the higher peak is for the difference in measured emission between the centre of the line and 2.5 MHz away from the centre; that with the lower peak is for the difference in measured emission between 2.5 MHz and 20 MHz from the centre of the line. The high rotational lines are sensitive functions of temperature; a 1% change in upper stratospheric temperature produces a 5% change in emission at the centre of the 27- line[2]. The instrument described here can measure upper stratospheric temperature variations with r.m.s. accuracies of ~ 1 K for an integration time of 1 h. Stratospheric phenomena which can be conveniently studied from the ground by this measurement technique include diurnal temperature variation[28] and sudden warmings[29].

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Genetic Control of Mitochondrial Enzymes in Human–Mouse Somatic Cell Hybrids

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The two techniques for detecting human enzymes in man/mouse cell hybrids described here provide a promising and interesting approach to the mapping of chromosomal genes coding for mitochondrial enzymes. The authors confirm the nuclear gene specification of citrate synthase and malate dehydrogenase, and give information on their possible linkage with each other and with other genetic markers.

MITOCHONDRIAL biogenesis depends on an interaction between the genetic activities of nuclear and mitochondrial DNA. The study of this interaction ideally requires a genetic system in which both chromosomal and mitochondrial segregation can be observed. Until recently these requirements were fulfilled chiefly by the lower eukaryotes: yeasts[1], Neurospora[2], Paramecium[3] and Tetrahymena[4]. Here we describe the first results of a coordinated study of mitochondrial biogenesis using somatic cell hybrids.

Somatic cell hybrids, especially man–mouse and man–Chinese hamster, have been used to map human chromosomes[5,6]. The presence of human enzymes, or non-enzyme proteins, which are electrophoretically distinguishable from their mouse or hamster homologues, can be correlated with the presence of other enzymes or proteins and specific chromosomes after the loss of human chromosomes. Theoretically, segregation of the mitochondria of the two parent species could be observed as well as interaction of the organelle of one species with at least some nuclear coded products of the other.

We have examined nine independently isolated man–mouse hybrid lines for the presence of two mitochondrially located[7] human enzymes that are usually assumed to be nuclear coded: NAD malate dehydrogenase (E.C. 1.1.1.37) and citrate synthase (E.C. 4.1.3.7). Where the usual electrophoretic methods could not separate human from mouse enzymes, immunological techniques were used to identify the human enzymes. Our studies confirm the nuclear control of these enzymes and give information on their possible linkage with each other, and with other genetic markers. The hybrids were also examined for the presence of a large number of other human enzymes (our unpublished results obtained in collaboration with H. Harris, D. Hopkinson, S. Povey and their colleagues).

Two groups[8,9] have shown that all the human–mouse hybrid lines examined by them (ten in all) had apparently lost the human mitochondrial DNA, whilst retaining the mouse component. Three of the hybrid lines we analysed were amongst those shown by Clayton et al.[8] to have no human mitochondrial DNA detectable by CsCl centrifugation.

Citrate synthase (CS) and NAD-malate dehydrogenase (MOR) are consecutively acting enzymes of the citric acid cycle, found in the mitochondrial matrix[7]. CS is thought to occur only in mitochondria, whereas MOR has a cytoplasmic counterpart (sMOR) which is apparently coded for at an independent nuclear locus[10,11].

Cytoplasmic sMOR is easily separated by electrophoresis from mitochondrial mMOR in both mouse and man, and the sMOR of the two species is also electrophoretically distinguishable (Fig. 1). Citrate synthase from the two species can now also be resolved by electrophoresis (as found by Craig[24]) on 'Cellogel' strips (Reeve Angel cellulose acetate).

We have not been able to separate mouse from human mMOR by electrophoresis in any of several buffer systems between pH 5.2 and 9.0 on polyacrylamide, starch or 'Cellogel'. This same problem has also arisen with a number of other mitochondrial enzymes, as discussed later, and has forced us to consider other approaches to distinguishing human and mouse enzymes.

One approach to this problem would be the analysis of hybrids involving one parent which is either heterozygous or homozygous for an electrophoretically mutant form of mMOR. Such mutants, however, are not available in mouse inbred strains[12] and thus, so far, in cell lines; and in a human population studied by Davidson and Cortner[10] the frequency of heterozygotes for an electrophoretic variant of mMOR was only 1%.

Immunological Approach

The use of immunological methods to distinguish human and mouse enzymes and other proteins provides another general approach to the study of human markers.

Specific antisera to human proteins or enzymes that do not cross-react with the mouse counterparts of these proteins can be obtained by immunizing mice with the appropriate human material. In the case of enzymes, these sera can be used for identification of human enzyme by immunodiffusion or immunoelectrophoresis followed by specific staining for the relevant enzyme. This procedure has been used to screen hybrids for the presence of human mMOR.

Human mMOR was purified from placental mitochondria prepared essentially by the method of Freeman[13] but omitting the sucrose gradient step. The mitochondria from a 1 kg placenta, suspended in 7.0 ml. 0.3 M sucrose–0.002 M EDTA–0.03 M nicotinamide–0.5% 'Triton' X-100, were sonicated for 4 × 30 s. The sonicate was spun and the supernatant layered onto a

5×15 cm column of 'Amberlite' CG50 equilibrated with 0.025 M sodium phosphate buffer pH 7.0 (ref. 14). The column was washed with 300 ml. of the equilibrating buffer to remove contaminating sMOR activity, and then with 600 ml. of 0.2 M sodium phosphate pH 7.0 to elute the mMOR. Fractions with malate dehydrogenase activity, assayed as described by Englard and Siegel[15], were pooled and concentrated by Amicon ultrafiltration. The resulting sample, which was free of sMOR and contained 300 μg protein ml.$^{-1}$ and 30 units[15] per mg protein of malate dehydrogenase activity, was used as the immunizing antigen.

A sample of human sMOR was prepared by the same ion exchange procedure using the supernatant fractions from the same placental preparation.

As the mouse parent in most cell hybrids examined was an 8-azaguanine resistant L cell (1R)[16] immunization was carried out in C_3H mice, the inbred line from which L cells were derived. The first subcutaneous injection into four sites was 0.4 ml. of $1:1$ v/v emulsion of antigen with Freund's complete adjuvant. Four weeks later, and subsequently at intervals of 1 week, booster injections were given in the same manner but using incomplete adjuvant for the emulsification. Immediately before each boost the mice were bled from the tail and serum was prepared. The sera were titred by double diffusion in agar against the original antigen. When a good titre was attained, the mouse was given an intraperitoneal injection of antigen and 10×10^6 live sarcoma S180 cells[17]. The relatively large volume of ascites fluid, produced within 7–10 days in response to the sarcoma, was of lower titre but yielded greater total antibody activity (by about a factor of 5) than could the available serum. When necessary, the sarcoma fluid was concentrated by dialysis against 18% sodium sulphate for 8 h, dissolving the precipitate formed in water, and dialysing at 4° C against phosphate buffered saline. Sera from different mice or different bleedings were not pooled.

Hybrid cells were grown in 'Biocult' RPMI 1640 medium supplemented with 10% foetal calf serum and the components of Littlefield's HAT selective medium, hypoxanthine, thymidine and amethopterin[16]. Mouse and human cell lines were grown in the same medium but without the HAT components.

Cell extracts were made by sonicating $40-50 \times 10^6$ cells in 0.45 ml. lysis buffer (5×10^{-2} M phosphate, 1×10^{-3} M mercaptoethanol, 2×10^{-5} M NADP, pH 7.0) for 10 s. The sonicates were clarified by a 1-min spin in a Beckman 'Microfuge' and stored in aliquots in liquid nitrogen. Their total malate dehydrogenase activity was measured spectrophotometrically[15] and adjusted to comparable levels where necessary.

Enzyme Activity of Hybrid Lines

The hybrid lines whose parentage is described in Table 1 were examined for: (i) citrate synthase activity by electrophoresis on 'Cellogel' (recently found by Craig[24]); (ii) NAD-malate dehydrogenase activity, also by electrophoresis; (iii) human mMOR activity by immunodiffusion using specific antiserum; (iv) a large number of other enzymes by electrophoresis on starch (our unpublished results obtained in collaboration with H. Harris, D. Hopkinson, S. Povey and their colleagues); and (v) chromosomes.

The electrophoretic pattern obtained for citrate synthase using extracts from some of the hybrid lines is shown in Fig. 2. In addition to the mouse citrate synthase band, which is seen in all the lines, some hybrids have another band of activity intermediate in mobility between that shown by the two parental lines. This intermediate band most probably represents a heteropolymeric molecule ($A^M A^H$) produced by the random interaction, in proportion to their concentrations, of mouse (A^M) and human (A^H) subunits. These patterns were consistent and reproducible in repeated runs with extracts from the same cell lines. The lesser staining activity of the hybrid band may be caused by reduced activity of the heteropolymeric enzyme in the hybrid cell or, more likely, unequal

production of human and mouse subunits because of a gene dosage effect. Such unequal production is most simply explained by extensive human chromosome loss during the evolution of the hybrid lines. This will usually leave only one copy of the human gene in the hybrid whilst most if not all of the heteroploid mouse parent's chromosomes will be retained, possibly leaving several copies of the corresponding mouse gene. Similar results have been observed before for other enzymes[18].
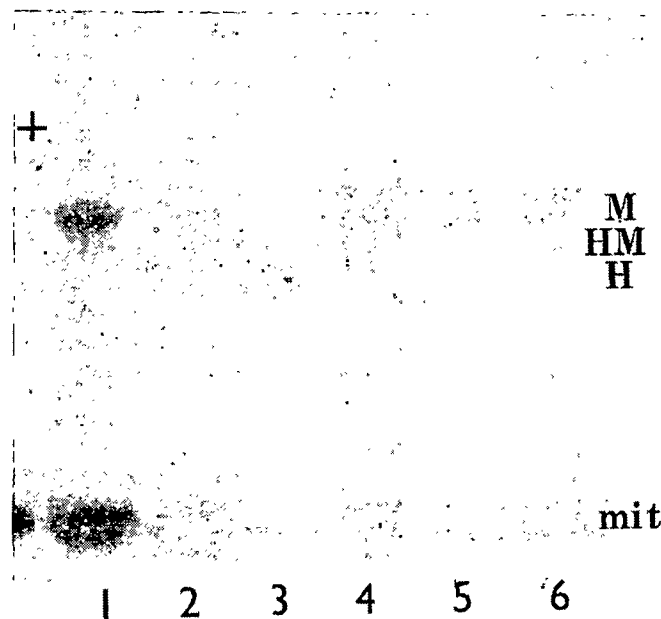
Fig. 1 NAD-malate dehydrogenase electrophoresis on 'Cellogel' (photograph of gel); 0.5 μl. samples were applied; the gel was run in 2.8 M sodium citrate–17.2 mM disodium hydrogen phosphate pH 7.0 buffer for 1.25 h at 200 V at room temperature. Stain: Total volume 2 ml. including 0.4 ml. 1 M Tris-HCl pH 8.0; 0.2 ml. 0.85 M malate pH 7.5; 10 μl. 0.05 M NAD$^+$; 50, μl. 1% thiazolyl blue (MTT); two crystals phenazine methosulphate (PMS). Identification of samples: 1, 4.42Z; 2, 4.12Z; 3, BREL; 4, HORP 3.2.1; 5, 1W1; 6, 1R. The arrow indicates the origin, and mit the mitochondrial enzyme band. H, HM and M refer respectively, to the human, human–mouse heteropolymer and mouse cytoplasmic forms.

An electrophoretogram stained for the MOR activity of extracts from some hybrids and controls is shown in Fig. 1. Mouse, human and hybrid extracts show indistinguishable cathodally migrating mMOR bands even when run for much longer times than shown. As has been reported before, however, by a number of workers[18,19], human and mouse sMOR can be resolved. Amongst the hybrids three have human as well as mouse cytoplasmic enzyme activity, again manifested only by a heteropolymeric band of intermediate mobility. As expected, all the hybrid lines examined show mouse sMOR activity.

Mitochondrial malate dehydrogenase was sought in the hybrid cell extracts by Ouchterlony double diffusion in agar, using the antisera produced in mice, as described above. Precipitin lines were visualized by staining for malate dehydrogenase activity using a tetrazolium system (Fig. 3). As expected after the precautions taken with the immunization procedure, and from published work on the relationship between sMOR and mMOR[20], no precipitin reaction was observed with the mouse lines 1R or 3T3, nor with human sMOR. The partially purified human mMOR (the immunizing antigen) gave a single, completely continuous precipitin line with the human lymphocyte line BREL (derived from the human parent in Z hybrids (Table 1, ref. 18)). No cross-reaction was found with a whole range of dilutions of commercial pig heart mMOR. This
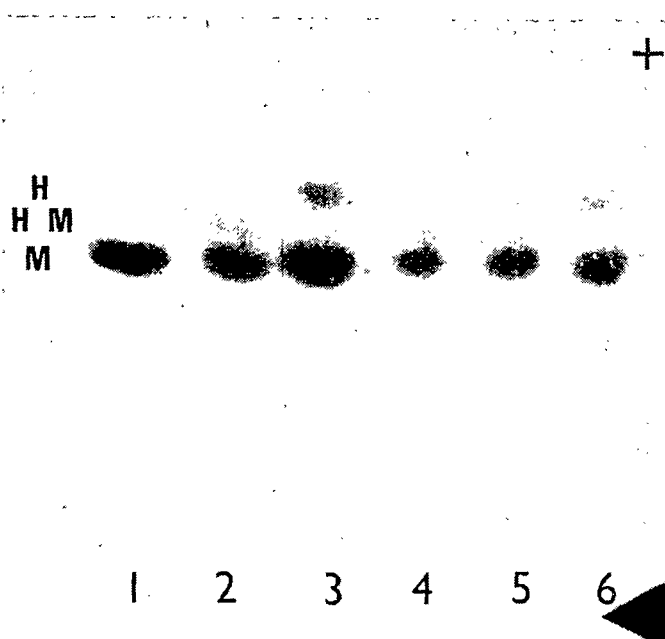
Fig. 2 Citrate synthase electrophoresis on 'Cellogel' (photograph of gel); 0.5 μl. samples were applied to 'Cellogel' strips and electrophoretic separation carried out in 0.1 M Tris adjusted to pH 8.0 with 0.1 M NaH₂PO₄, for 2 h at 150 V at room temperature. The staining mixture based on the reduction of dichlorophenol indophenol by reduced coenzyme A is to be reported elsewhere[24]. Identification of samples: 1, 4W10; 2, 3W4; 3, 1R+BREL; 4, HORP 3.2.1; 5, HORL 4.1; 6, 1R+BREL.

may mean that the precaution of immunizing mice to avoid cross-reaction is not necessary with this particular enzyme.

Lactate dehydrogenase (LDH) patterns were established by electrophoresis on 'Cellogel'[6]. The presence of human A and B subunits (the latter on the basis of quantitative differences only) was scored as described previously[18].

Table 1

Hybrid lines	Human parent	Mouse parent
1W1, 2W1, 3W4, 4W10 (ref. 16)	Normal lymphocytes (MAR)	1R, 8-azaguanine resistant L-cell
HORL 4.1, HORP 3.2.1	Normal lymphocytes HOW)	1R, 8-azaguanine resistant L-cell
Not previously examined, made as in ref. 16		
4.12Z, 4.31Z, 4.42.7Z (ref. 18)	Normal lymphocytes (BRE)	1T, bromodeoxyuridine resistant subclone of 3T3

The combined results of repeated testing of the nine hybrids for CS, mMOR, sMOR and LDHB—also peptidase B (our unpublished results obtained in collaboration with H. Harris, D. Hopkinson, S. Povey and their colleagues) because of linkage—are shown in Table 2, together with information on the presence of mitochondrial DNA where this is available.

Implications

Three principal implications for the control of the two mitochondrial enzymes are suggested by the data in Table 2. First, of the hybrid lines shown by CsCl isopycnic centrifugation[8] to have no human mitochondrial DNA, three were also studied by us. Of these, two have both the mitochondrial enzymes studied and one has neither. Thus we can conclude

that the presence of human mitochondrial DNA is not required for the expression of at least some human mitochondrial functions. Whether this is because there is no strong control by mitochondrial DNA on all the nuclear coded products which eventually become incorporated into the organelle, or because such control exists[2] but is not species specific, we cannot say on the basis of present data.

An interesting question which arises is whether the human nuclear coded mitochondrial enzymes produced in these hybrids are in fact located in the mitochondria which are presumed to contain only mouse mitochondrial DNA. The fact that a heteropolymeric band of citrate synthase is observed on electrophoresis of certain hybrids, but not when a mixture of human and mouse cell extracts is run together[24], suggests that in some location in the hybrid cell the human and mouse enzymes are found together. Supporting this deduction, preliminary results from immunodiffusion with sonicated mitochondria from sucrose gradient fractionation[13] of large quantities of 2W1 show that human mitochondrial malate dehydrogenase activity is located in the mitochondria of this hybrid line.
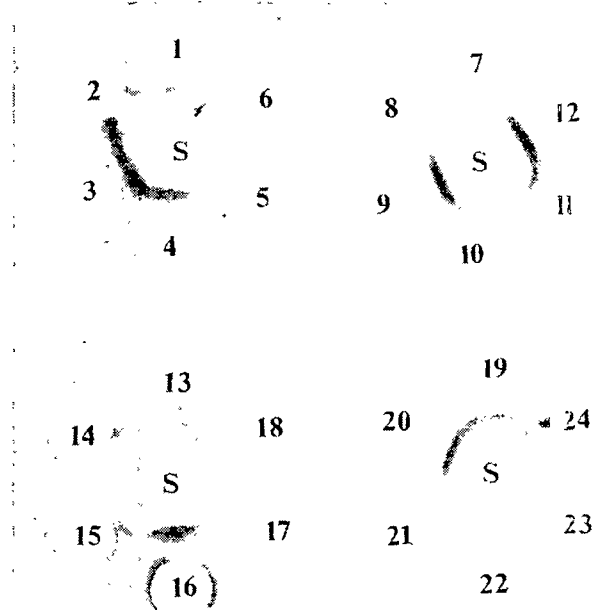
Fig. 3 Ouchterlony double diffusion in agar, using the specific mouse anti-human mMOR serum, stained for malate dehydrogenase activity. Supporting medium: 1.5% Nobel agar in 0.9% NaCl solution. 6 μl. cell extract per well used. Diffusion took place for 36 h at 4° C. Slides were washed in 0.9% aqueous NaCl for 24 h at 4° C. Staining as for 'Cellogel'. S in the centre well refers to the antibody containing sarcoma induced ascites fluid. Identification of other wells: 1, BREL (38.7); 2, sMOR; 3, mMOR immunizing antigen (59.7); 4, 2W1 (139.8); 5, 1R (212.4); 6, 1W1 (120.6); 7, 1R; 8, HORL 4.1 (147.0); 9, mMOR; 10, 4W10 (138.6); 11, BREL; 12, 3W4 (139.8); 13, BREL; 14, 4.42Z (140.4); 15, 3T3 (179.4); 16, 4.31Z (166.8); 17, 3T3; 18, 4.12Z (141.6); 19, BREL; 20, mMOR; 21, sMOR; 22, HORP 3.2.1 (127.2); 23, 1R; 24, HORP 3.2.1. Numbers in brackets give malate dehydrogenase activities in 6 μl. of cell extract, in units × 10³ (ref. 15).

The second feature of the data is the absence of a specific relationship between the expression of cytoplasmic and mitochondrial malate dehydrogenase in the hybrid cells examined. This is in agreement with genetic data on mutant forms of both enzymes in man and mouse[10-12]. It is worth mentioning that the three hybrids that have sMOR activities are also the only ones showing cytoplasmic NADP isocitrate dehydrogenase activity, an association that is consistent with the suggested linkage between these two functions[21].

The third and perhaps the most striking feature of the data of Table 2 is that there seems to be a strong positive correlation between the presence of human citrate synthase and mitochondrial malate dehydrogenase in the hybrid lines examined. The unrelated enzyme functions LDHB and peptidase B, the loci for which are linked to each other and are probably on chromosome 12 (ref. 19), also show a marked positive correlation with the expression of CS and mMOR. In fact, the only exception to a complete correlation between the presence and absence of these four enzymes, which is expected if they are all controlled by genes on the same chromosome, is the hybrid line 2W1. None of the other 28 enzyme activities tested for (our unpublished results obtained in collaboration with H. Harris, D. Hopkinson, S. Povey and their colleagues) showed any obvious association with any of these four enzymes. Of the total of thirty-two enzyme activities that were studied, 2W1 shows only mMOR and the X-linked activities hypoxanthine guanine phosphoribosyltransferase (HGPRT), phosphoglycerate kinase (PGK) and glucose-6-phosphate dehydrogenase (G6PD). These X-linked functions are expected to be present because the human X chromosome is selectively retained in these hybrids in the HAT medium. It is tempting to suggest that the four enzyme CS, mMOR, LDHB and peptidase B are all controlled by genes on the same chromosome, presumably number 12, and that 2W1 contains only a fragment of this chromosome perhaps, for example, just one arm. In this case this fragment must carry the gene for mMOR but not the other three genes. A complete karyotypic study of 2W1 is under way, but preliminary observations do suggest that 2W1 retains perhaps at most one recognizable human chromosome other than the X.

Table 2 Mitochondrial Enzyme and Other Activities in Nine Different Human–Mouse Hybrids

Hybrid cell line	CS	mMOR	sMOR	mitDNA	LDHB/ pepB
1W1	−	−	−	NT	−
2W1	−	+	−	NT	−
3W4	+	+	−	−	+
4W10	−	−	−	−	−
HORL 4.1	−	−	−	NT	−
HORP 3.2.1	+	+	+	NT	+
4.12Z	±*	+	+	−	+
4.31Z	+	+	−	NT	+
4.42.7Z	−	−	+	NT	−

+, Presence of human activity; −, absence; NT, not tested.

*, Very weak activity possibly because of an extreme gene dosage imbalance, as 4.12Z has a doubled chromosome complement from its mouse parent, 3T3.

CS, Citrate synthase; mMOR, sMOR are respectively mitochondrial and cytoplasmic NAD-malate dehydrogenase; mitDNA, mitochondrial DNA; LDHB, lactate dehydrogenase subunit B; pepB, peptidase B.

Only the presence of human activities and mitDNA in the hybrid lines is recorded in this table. In all cases, however (except for mMOR), the mouse component is invariably present. In the case of mMOR the immunological technique used so far scores only for the human activity.

In the course of screening electrophoretic properties of mitochondrial enzymes the difficulty of separating mouse and human forms in the case of several enzymes was striking. Others have encountered similar difficulties (refs. 6, 10 and our unpublished results obtained in collaboration with H. Harris, D. Hopkinson, S. Povey and their colleagues). We find that the mitochondrial component at around physiological pH migrates only a short distance to one or other side of the origin, and is always more cathodal than the cytoplasmic enzyme.

Whether because of these characteristics, or because there is a strong selective conservation of charge properties amongst these enzymes (MOR, GOT (glutamate oxaloacetate transaminase), IDH (NADP isocitrate dehydrogenase)), it is difficult if not impossible to separate mouse and human components sufficiently to allow hybrid analysis by electrophoretic means. The immunological approach may therefore find more widespread use in these obstinate cases. Conservation of charge amongst these mitochondrial enzymes is perhaps also suggested by the low frequency of electrophoretic variants in the populations so far examined[22]. It is not impossible that the similar and apparently invariable charge of these enzymes at physiological pH values is a requirement for their localization in mitochondria.

There are exceptions to this suggested charge conservation. Mitochondrial NADP malate dehydrogenase migrates to the anode in the mouse and to the cathode in man at pH 7.0[12,23]. But this enzyme shows a high frequency of polymorphism (30% heterozygotes for the variant) in the populations that have been examined[23].

The results of this study demonstrate once more the power of somatic cell hybridization as a tool for a combined genetic and biochemical analysis of eukaryotic systems. We have confirmed the nuclear gene specification of two mitochondrial enzymes, citrate synthase and malate dehydrogenase, and established a possible linkage between them and with the enzymes LDH-B and peptidase B on chromosome 12. We have also confirmed the genetic independence of the mitochondrial and supernatant forms of malate dehydrogenase. If our genetic interpretation is correct, then it is probable that the genes for CS and mMOR are not clearly linked, so that this linkage may have no special functional significance. Further work is in progress to extend this analysis to other mitochondrial enzymes, and to proteins and other gene products that are likely to be coded for by the mitochondrial DNA.

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LETTERS TO NATURE

PHYSICAL SCIENCES

New Kind of Ring Around Saturn?

TITAN, a satellite of Saturn, is the only satellite in the Solar System known to possess an atmosphere. That such a small body, only 87% more massive than the Earth's Moon and with a diameter but 40% larger[1], should have an atmosphere is a mystery to which Sagan[2] may have provided an answer—outgassing of the satellite. But barring extraordinary circumstances, the satellite must lose its atmosphere at a prodigious rate. But what happens to the atmosphere after it leaves Titan?

What is remarkable about the ejected atmosphere is that, although it has Titanian escape velocity, it probably does not have Saturnian escape velocity. Trafton[3] has estimated the exospheric temperature of Titan to be 74 K. At that temperature, even hydrogen atoms have an r.m.s. thermal speed of only 1.4 km s^{-1}. Because Titan's orbital speed about Saturn is 5.6 km s^{-1}, the average ejected hydrogen atom will not reach the Saturnian escape velocity of 7.9 km s^{-1} (at Titan's orbit) even if ejected forwards. Consequently, atoms and molecules lost by Titan are forced by the planet's gravitational field to orbit Saturn until ionized or until they are recaptured by Titan, forming a gaseous torus encompassing Titan's orbit. Once ionized, they will be swept away by the solar wind, unless Saturn has a magnetosphere extending to Titan's orbit.

The composition of the Titanian atmosphere is believed[2-5] to be either predominantly molecular hydrogen or a mixture of comparable amounts of hydrogen and methane. We assume the ejected hydrogen to be photodissociated into atomic hydrogen. The lifetime of an atom of hydrogen subject to solar wind charge-exchange ionization is about 6 yr or 140 Titanian orbital periods at the distance of Saturn[6-8]. The solar photoionization lifetime will be even longer[9]. Consequently, the torus can store a 6-yr supply of Titanian hydrogen. For a temperature of ~70 K, the torus will have a width, in the equatorial plane, of the order of the orbital radius of Titan, r_T, which is 20 Saturnian radii, and a thickness, normal to the plane, of ~$r_T/2$. We take the volume of the torus to be ~r_T^3, and use Trafton's Titanian escape rates[3] (2×10^{26} to 4×10^{29} molecules s^{-1}); we find that the density of the torus is ~40 to ~9×10^4 atoms cm^{-3}. A torus of these densities would probably be detectable from Earth orbit by resonantly scattered Lyman-α radiation, or by absorption during an occultation by the torus of an interstellar Lyman-α source. If Saturn has a magnetosphere, however, the density could be smaller because of charge exchange with magnetospheric plasma.

We estimate that, if the Titanian exospheric radius is the order of 10 Titanian radii, as in some of Trafton's models[3], more than 90% of the escaping atoms could be recaptured by Titan (which lowers the upper limit of toroidal density to ~2×10^3 cm^{-3}). Hence, the torus presents a mechanism which allows satellites previously thought incapable of possessing an atmosphere to have one, and it suggests a sensitive way of testing for atmospheres of distant satellites by Lyman-α observations. The outer planets, where the solar ionization rate is small, are most conducive to the existence of such gaseous toruses. A more detailed study of this problem is given by T. R. McD. and N. M. B. (to be published). Saturn, in particular, should be examined for a gaseous torus that is larger, in absolute dimensions, than the Sun.

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Apollo 17 Age Determinations

THE Apollo 17 mission landed in a valley in the highland region forming part of the south-eastern rim of the Sea of Serenity (20° 09' 50" N, 30° 44' 58" E). An early allocation of a limited number of samples has been made to provide preliminary information on this site and we report here the results of age determinations we have made on two crystalline rocks using the ^{40}Ar–^{39}Ar and ^{38}Ar–^{37}Ar dating techniques[1,2]. The description of sample documentation and relationship of samples to the geology at the Apollo 17 site is based on a preliminary report (Astrogeology 71) issued by the Apollo Lunar Geology Investigation team and may be subject to modification. Sample classification is based on information supplied by the Preliminary Examination team at the Manned Spacecraft Center.

The samples analysed were: (1) A coarse grained basalt, 75055, which was part of a rock fragment removed by astronaut Schmitt from a metre sized boulder on the rim of Camelot crater (station 5). 75055 consists of approximately 35% plagioclase, 45% yellowish brown pyroxene and 20% opaque minerals (ilmenite). The dominant grain size was around 1 mm and in the hand specimen the sample resembled the Apollo 11 low-K basalts. Preliminary examination of the samples from the vicinity of Camelot crater indicates that subfloor basalts covered this part of the valley floor to a depth of at least 100 m before formation of the crater. 75055 may be regarded as representative of this subfloor basalt unit. We have analysed a 50 mg rock chip of 75055. (2) A sample, 76055, described in the preliminary examination as a vesicular anorthositic gabbro. This sample was collected by the astronauts 3 km north of the

landing site, at station 6, near the base of the large mountain referred to as the North Massif. The anorthositic gabbro seems to be a principal rock type at station 6 forming a matrix to other types of brecciated samples. Preliminary examination at Houston indicates that the material is thoroughly recrystallized. Our sample of 76055 consisted largely of a greenish-grey fine grained matrix of plagioclase and smaller amounts of pyroxene with irregular lenses of pyroxene and plagioclase which appear in binocular microscope examination of the hand specimen to be a coarser grained version of the matrix. We have analysed a 70 mg chip of the matrix and a 19 mg chip of one of the lens-like clasts. At present we do not have a thin section description of either sample.

The samples were vacuum encapsulated in quartz ampoules and irradiated in the core of the Herald reactor, AWRE, Aldermaston. Three samples of a terrestrial hornblende Hb3 gr, described previously[2], were spaced around the lunar samples to monitor the conversion of ^{39}K to ^{39}Ar. ($^{40}Ar/$ ^{39}Ar) ratios, corrected for atmospheric ^{40}Ar and calcium derived ^{39}Ar, were measured for argon extracted from the three monitors as 15.11 ± 0.09, 15.04 ± 0.04, and 15.12 ± 0.06. The irradiation parameter, $J = (\exp (\lambda T) - 1)/(^{40}Ar/^{39}Ar)$, was thereby determined as 0.0501 ± 0.0010 ($T = 1.062 \pm 0.020 \times 10^9$ yr (ref. 2), $\lambda_\beta = 4.72 \times 10^{-10}$ yr^{-1}, $\lambda_e = 0.584 \times 10^{-10}$ yr^{-1}, $^{40}K/K = 0.0119$ atom %).

The samples were heated by a resistance heater in a gas extraction furnace for periods of 1 h at a sequence of temperatures up to 1,600° C. The argon evolved at each temperature step was cleaned by a heated Ti getter and analysed in a mass spectrometer. Atmospheric ^{40}Ar corrections were applied on the basis of furnace blanks measured before and after the introduction of samples to the furnace and are typically less than 1%. ^{39}Ar has been corrected for Ca derived ^{39}Ar (ref. 3). Both rocks contain cosmogenic and trapped (solar type) ^{38}Ar and ^{36}Ar. ^{40}Ar has been corrected for cosmogenic and trapped ^{40}Ar assuming ($^{40}Ar/^{36}Ar$) $= 1 \pm 1$ for both components. To calculate cosmic-ray exposure ages the proportion of cosmogenic ^{38}Ar has been calculated assuming ($^{36}Ar/^{38}Ar$) $= 5.25$ and 0.63 for trapped and cosmogenic components respectively.

Fig. 2 Argon release pattern for Apollo 17 anorthositic gabbro 76055. The age quoted is based on the major release (880° C and 980° C) only. ——, Matrix; — — —, clast. $T = 3.98 \pm 0.05$ aeons.

In Figs. 1 and 2 we present the ($^{39}Ar/^{37}Ar$) ratio and the corrected ($^{40}Ar/^{39}Ar$) ratio plotted as a function of the proportion of ^{39}Ar released. We also show the (K/Ca) ratios and apparent K-Ar ages to which the argon isotope ratios correspond (see, for example, ref. 3).

The argon release pattern of 75055 is quite similar to patterns observed previously in lunar basalts[4,5]. The low ($^{40}Ar/^{39}Ar$) ratio in the initial release indicates a small loss of ^{40}Ar (12%), probably as a result of solar heating, and the corresponding ($^{39}Ar/^{37}Ar$) ratio indicates that the loss is associated with potassium rich sites, probably an interstitial K-rich glass phase[6,7]. On the basis of the high temperature release, an age of 3.75 ± 0.05 aeon is deduced for 75055.

Fig. 1 Argon release pattern for Apollo 17 subfloor basalt 75055. The temperatures are extraction furnace temperatures. The 1,300° C fraction contains a large (2%) and uncertain correction for cosmogenic ^{40}Ar. $T = 3.75 \pm 0.05$ aeons.

Table 1 Representative ^{40}Ar–^{39}Ar Ages of Lunar Samples

Sample type	Age (aeon)	Reference
Mare type basalts		
A11, high K	3.56 ± 0.09	4, 5
A11, low K	3.83 ± 0.09	4, 5
12002, 12051, 12065 (A12)	3.26 ± 0.06	5
15555 (A15)	3.31 ± 0.03	10
75055 (A17)	3.75 ± 0.05	This communication
Highland samples		
12013 (A12, "granitic" breccia) *	4.03 ± 0.07	5
14310, 14073 (A14, basalt)	3.88 ± 0.05	2, 7
14053 (A14, basalt)	3.95 ± 0.05	2
15382 (A15, KREEP basalt)	3.90 ± 0.05	†
15415 (A15, anorthosite)	4.05 ± 0.15	3
62295 (A16, norite)	3.87 ± 0.05	†
67075 (A16, anorthosite)	4.06 ± 0.05	†
L2015 (Luna 20, 8 mg. anorthosite fragment)	4.0 ± 0.3	†
76055 (A17, anorthositic gabbro)	3.98 ± 0.05	This communication

* The unique rock 12013 is listed with the highland samples somewhat arbitrarily on the basis of its age.

† D. T., T. H. C. and C. J. Y., presented at the 4th Annual Lunar Science Conference and submitted for publication in the *Proceedings* (1973).

The age of 75055 is comparable to the average age, 3.84 ± 0.09 aeon, determined previously for three Apollo 11 low-K basalts (Table 1), and confirms that the period of extrusion of

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mare basalts on the Moon began as early as 3.8 aeon. The absence of intense cratering in the basalt flows at the Apollo 17 site places constraints on the early bombardment history of the lunar surface. For example the Imbrium event must have occurred before 3.75 aeon. We have argued elsewhere that this event occurred at 3.89 aeon (†, legend to Table 1).

The argon release pattern of 76055 does not show effects of appreciable argon loss but does have some structure. The initial release of both matrix and clast shows a high (^{40}Ar/^{39}Ar) ratio whereas in the high temperature release from the matrix the ratio decreases. Similar effects have been observed in Apollo 14 breccias[2] and are not fully understood. The effects in 76055 are relatively small and over most of the release pattern the (^{40}Ar/^{39}Ar) ratio is not significantly different from the overall ratio. An age of (3.98 ± 0.05) aeon is calculated for both samples based on the major release at 880° C and 980° C. The ages based on the overall release are 3.96 aeon and 3.99 aeon for matrix and clast respectively. From a comparison of the (^{39}Ar/^{37}Ar) release patterns it is clear that the chemistry of both samples was very similar.

The age of 76055 is compared to the ages determined for highland material returned by earlier missions in Table 1. The concentration of ages around 4.0 aeon and the absence of ages in the period 4.0 to 4.6 aeon are the most obvious features of the distribution of ages which must be accounted for. Two classes of hypothesis may be put forward to explain the age pattern. The intense bombardment of the lunar surface in the period 4.0 to 4.6 aeon may have been responsible for heating and consequent argon loss from the highland samples. The predominance of clastic rocks and evidence of recrystallization in many of the highland rocks lend support to such hypotheses. The heating effects responsible may indeed be dominated by a small number of very large impacts in the regions visited specifically the Imbrium event and (for Apollo 17) the Serenitatis event. The location of the Apollo 17 site in the highlands surrounding the Sea of Serenity raises the possibility that the age of 76055 may indicate the time of the Serenitatis impact.

The possibility of explaining the age distribution in terms of the heating effects associated with capture of the Moon by the Earth cannot be ruled out for the period 4.6 to 4.0 aeon but the capture hypothesis and its associated tidal effects must face the additional constraint of the circularity of lunar craters[8].

A second class of hypothesis regards the ages as true crystallization ages resulting from melting in the subcrustal regions as a result of internally generated heat. The ages of the mare basalts are usually accounted for as crystallization ages[4,6]. Although such hypotheses may not be realistic as applied to the ages of clastic rocks it may still be possible to explain the anorthosite ages in this way[3]. The significance of the anorthosite ages is crucial to an understanding of early lunar history but at the present time is an open question. Both classes of hypothesis must satisfy the evidence from Rb-Sr measurements (such as rock 12013) for the early formation of a radioactive lunar crust 4.5 aeon ago[9].

We have determined cosmic-ray exposure ages for 75055 and 76055 on the basis of the ratio of cosmogenic ^{38}Ar to ^{37}Ar produced artificially from Ca[2,3]. The corresponding (^{38}Ar/Ca) ratios are: $(1.38 \pm 0.06) \times 10^{-6}$ ml. (STP) g^{-1} for 75055 and $(1.91 \pm 0.10) \times 10^{-6}$ ml. (STP) g^{-1} for both clast and matrix of 76055. The corresponding exposure ages, based on a nominal ^{38}Ar production rate of 1.4×10^{-8} ml. (STP) g^{-1} m.y.$^{-1}$ (ref. 2), are: 98 ± 5 m.y. (75055) and 136 ± 7 m.y. (76055).

The exposure ages are a measure of the integrated irradiation history of the samples. 76055 was a small rock lying on the mountain slope at station 6 and has no clear relationship to any cratering event in that vicinity. We can infer no immediate conclusions from our measurement of its exposure age but must await a more statistically significant number of measurements on material from station 6. By contrast 75055 seems to be clearly associated with the impact which produced Camelot crater and we therefore infer an age of (98 ± 5) m.y. for the age

of Camelot. A number of crater ages have now been determined on the Apollo missions (Apollo 14 Cone crater, 26 m.y. (ref. 2); Apollo 16 North Ray, 46 m.y. (†, see legend to Table 1); Apollo 17 Camelot, 98 m.y.) and provide a fairly well defined absolute time scale with which to compare relative ages based on crater morphology.

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Note added in proof. Since the paper was written a duplicate analysis of 75055 has yielded results identical to those presented here.

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Orange Soil from the Moon

THE discovery of an orange-coloured soil on the Moon by the Apollo 17 astronauts last December led to much excitement and speculation. Dr Jack Schmitt, the geologist on the mission, realized that such yellow to orange coloration in rocks on Earth is usually due to hydrated iron oxides. In a volcanic region, these minerals are produced from water-rich vapours reacting with the lavas and emanating from gas-vents or "fumaroles" associated with the volcano.

Before this discovery, all the evidence from lunar volcanic rocks pointed to the absence of water (except possibly as a transient phase quickly lost from the lunar environment due to the low gravitational field). The rarely discovered hydrous minerals (such as goethite) were confined to a few of the rocks fragmented by meteoritic impact (breccias), and there is additional evidence that certain classes of external meteorite, such as carbonaceous chondrites, as well as comets, could contribute water as well as other volatile constituents to the lunar soils and breccias. Dr Schmitt was on the alert for evidence of recent volcanism in the Taurus-Littrow region, in view of some morphological evidence in support of that possibility. His conclusion while on the Moon was that Shorty crater could be associated with young volcanic activity and that the orange coloration in the adjacent soil was perhaps due to fumarolic activity. Scientists on Earth concluded that, if this were so, oxidation of the iron-minerals in the lava debris implied the presence of water in the lunar interior, perhaps up to recent times, which was released to the surface during volcanic eruptions. If so, and the water remained long enough to react with the surface lavas, then the role of water during earlier processes on the Moon would be more significant than had been envisaged.

We were allocated a small sample of orange soil (0.25 g) together with a basaltic lava specimen which reached Durham on February 24, and we presented our data and conclusions at the Fourth Lunar Science Conference in Houston (March 8). In this communication we show how it was possible to reach a precise conclusion from chemical analysis, and to clarify the situation regarding the orange soil. We conclude that the material was not produced by volcanic processes.

The soil sample (74220,60) consists almost entirely of tiny glassy spheres or beads (average diameter 0.1–0.2 mm); they range from pale yellow to black in colour, but are predominantly orange. Less than 5% of the sample consists of mineral fragments, chiefly plagioclase feldspar. Electron probe analysis of spheres of varying colour gave the compositions in Table 1. The orange colour is almost certainly due to the high titanium content, as similar orange glasses from other missions show high TiO_2 values. The content of TiO_2 is not, however, the most remarkable feature of these glasses, as some of the mare basalts from Apollo 11 and Apollo 17 sites show higher contents. The unusual feature is the low aluminium, giving Al_2O_3 values much lower than in basaltic lavas. Calculation of the normative mineral contents of the glasses, for example (Table 1), shows only 14.3% to 17.4% normative plagioclase feldspar. Conversely, the normative contents of mafic minerals are very high, with up to 43% normative olivine in the black glassy spheres. This unusual composition can best be explained as due to the melting of mineral debris on the lunar surface by meteorite impact, giving splashes of liquid droplets. A similar origin has been advocated for glassy beads from previous mission collections, where the beads include feldspathic (colourless) and pyroxenitic (green) compositions.

Table 1 Apollo 17 Orange Glass (74220,60) with Comparisons

	Typical orange*	Range	Black glass †	Apollo 11 orange glass	Mare 4 basaltic glasses
SiO_2	38.98	37.8–39.0	38.06	42.21	37.64
TiO_2	9.23	8.9–9.6	7.26	8.47	12.04
Al_2O_3	5.67	5.6–5.7	4.77	11.32	8.46
FeO	22.44	22.2–22.8	22.57	16.87	19.93
MnO	0.24	0.24–0.28	0.28	0.20	ND
MgO	14.47	13.8–15.1	20.40	8.67	10.49
CaO	7.31	7.1–7.5	5.57	10.86	8.81
Na_2O	0.43	0.34–0.43	0.30	0.28	0.54
K_2O	0.04	0.04–0.04	0.04	0.21	0.13
Cr_2O_3	0.66	0.63–0.72	0.66	0.32	0.48
Total	99.47		99.91	99.41	98.52

* Typical of yellow, orange, red–brown and some black glasses.

† Example of some black glasses that are heterogeneous and variable.

Typical orange norm: Or 0.24, Ab 3.66, An 13.49, Di 18.79, Hy 24.10, Ol 21.12, Cm 0.97, Ilm 17.62.

Norm minerals (black): Plag 14.3 (An81), Cpx 13.1, Opx 14.9, Ol 42.9 (Fo69), Opaques 14.8.

Norm minerals (orange): Plag 17.4 (An78), Cpx 18.8, Opx 24.1, Ol 21.1 (Fo65), Opaques 18.6.

Approximate relations: 100 parts orange + 38 parts olivine = black.

The glassy spheres are generally free from residual crystals that could be attributed to the impacting body (no nickel-iron particles, for example). They do, rarely, contain fragments of ilmenite (suggesting residual grains from the impacted source rocks) and minute feathery crystals of ilmenite (orange glasses) or olivine (black glasses) suggestive of the melt being oversaturated in these components, and hence they were expelled first during devitrification.

An X-ray fluorescence analysis of the bulk soil sample was then undertaken, using a non-destructive method. The results (Table 2) are surprising in that the contents of zinc, copper and nickel are extremely high. This is particularly strong, further evidence against the notion that the glass beads could be due to volcanic eruption of basaltic liquid in the form of fountain droplets. Trace element data are not yet available for the Apollo

17 basalts, but their mineralogy and major-element chemistry indicate very close similarities to the Apollo 11 titaniferous mare basalts. A comparison (Table 2) shows that such basalts have extremely low contents of Zn, Cu and Ni (an Apollo 17 basalt contains Ni-free iron also). In fact, the "orange soil" is even richer in Zn and Cu than the Apollo 11 soil which contains meteoritic debris as well as local basalt fragments.

Table 2 Orange Glass Sample (74220,60). Semi-quantitative, Non-briquetted (0.25 g) XRF Analysis (p.p.m.)

	Orange sample	Apollo 11 basalt (10045)	Apollo 11 soil (10085)
Ba	88	44	257
Nb	10	12	15
Zr	170	219	351
Y	45	85	124
Sr	179	145	159
Rb	<1	1	3
Zn	262	3	19
Cu	42	6	16
Ni	65	4	117

We conclude, therefore, that the impacting material was unusually rich in Zn and Cu, and that it has been dissolved in the liquid produced by the impact event. Evidence presented at the recent Houston conference by other investigators indicates that cometary impact may be responsible for high levels of zinc and chlorine in Apollo 16 rocks, and therefore the unusual abundance of glass beads at the Apollo 17 site may be due to this type of impact. Although our evidence is aimed at distinguishing between impact and volcanic processes, other investigators reported data relevant to the two other problems raised by Dr Schmitt's observations. Analysis by Mössbauer spectroscopy showed the absence of ferric iron in the orange glasses (and hence a low oxidation state), and isotopic measurements showed the materials not to have been formed by recent events on the Moon. Hence we have no evidence for young, hydrous volcanism on the Moon and the orange and black soil seems to be a local, strong concentration of impact-generated melts.

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Lunar Tides and Magnetism

RECENT observations and studies of the lunar surface based on Apollo and Explorer flights[1] show that some rocks brought to Earth are magnetized, that there are on the Moon weak, local, fairly randomly oriented magnetic fields but no overall poloidal field, that the magnetic perturbation of the solar wind by the surface of the Moon as observed by lunar orbiters is concentrated at latitudes lower than about 40° (ref. 2) and, finally, that the chemistry of the surface suggests high present and past radioactivity[3]. Here I propose a model, based on these observations, which may lead to the understanding of the origin of lunar magnetism a few billion years ago.

It has been pointed out[1] that the observed lunar magnetism cannot be accounted for either by terrestrial or by solar magnetic fields. The possibility that the Moon once had a sufficiently hot liquid core in which a turbulent convective motion could have produced a magnetic dynamo driven either by a thermal gradient[4,5] or by precession[6] seems to be marginal for energetic or electromagnetic reasons[7]. The existence of a

liquid core is also in seeming conflict with the dynamic stability of the Moon[8]. It is interesting, therefore, to inquire whether a magnetic field could have been generated in an outer liquid shell. The studies of Gast[9] and Wood et al.[3] of the lunar composition and of its present and past radioactivity lead to the conclusion that at an early epoch, some 3 to 4×10^9 yr ago, there existed a thin anorthosite crust (density 2.9 g cm^{-3}) which was floating on a few hundred kilometres thick layer of molten gabbro (density 3 to 3.3 g cm^{-3}) which, in turn, was supported by solid olivine (density 3.2 to 4.4 g cm^{-3}). This transient situation was caused presumably by a relatively brief pulse of heat generated by various short-lived radioactive elements, primarily [26]Al, which tended to concentrate in the liquid fractions.

If such an external liquid shell indeed existed then, in principle, a magnetic field could have been generated in it either by thermally driven convection in analogy to what has been suggested for Jupiter[10,11], or by tidal motions produced by Earth[7]. In order to assess the validity of these two mechanisms it is necessary to estimate first the average velocities v produced in the liquid. Using Fish et al.'s[12] numerical values for [26]Al and for its initial concentration in a 100 km thick layer, the layer must have become liquid in a few million years and at that time the outward heat flux Q was of the order 10^4 erg s[-1] cm^{-2} implying a surface temperature of about 100 K if no other heat source was present. The simple mixing length theory of thermally driven convection[13] with the appropriate numerical quantities leads to the expression

$$v^3 = 8 \times 10^{-9} l \ Q \ cm^3 \ s^{-3}$$

With a mixing length l of the order of 1 to 100 km convective velocities are 2 to 10 cm s^{-1}. Radioisotopes other than [26]Al would lead[12] to much later melting, lower heat fluxes and lower convective velocities.

For evaluation of the tidal mechanism I assume that the outside crust is so thin that it is easily deformable and does not affect the motions in the liquid. The perturbing potential relative to the Moon produced by Earth in the liquid shell at a point P on the lunar surface[14] is

$$\Omega = (3/2)\gamma \ Er^2 \ D^{-3} \ (1/3 - \cos^2 \theta) \qquad (1)$$

where γ is gravitational constant, E is mass of the Earth, r is radius of the Moon, D is distance between Earth and Moon and θ is the angle between the line joining the centres of the two bodies and the lunar radius leading to point P (or approximately the lunar latitude). The average value of the perturbing force field (radial and tangential)

$$\overline{\nabla \Omega} \sim (3/2) \ \gamma \ Er \ D^{-3} \qquad (2)$$

is about 2×10^{-3} cm s^{-2}, some 23 times larger than the corresponding lunar gravitational field responsible for tides on Earth. It follows that the solar influence, which on Earth is comparable to the lunar influence, is negligible for the Moon. The problem of evaluating velocities v in tidal motions even in a liquid layer of uniform thickness is a formidable one. But an approximate estimate of an average velocity v can be made applying to a spherical shell Malkus's[6] assumption that the perturbing force is of the same order of magnitude as the Coriolis force per unit mass $|2 \ \omega \times v|$ where ω is angular velocity. If at the early epoch the rotation of the Earth and the Moon had not yet been slowed, both could have had a period of less than 10 h, typical of initial periods of most bodies in the Solar System[16,17]. On the other hand, the very low dynamic symmetry of the Moon may have existed at that time and may already have affected its rotation so that longer periods should be also considered. For periods between 10 h and 30 day the corresponding velocities are 6 to 400 cm s^{-1}.

A self-sustaining magnetic dynamo can exist[10] if the magnetic Reynolds number $G = \mu L \sigma v$ is greater than 10. Here μ is permeability, L is linear dimension and σ is electrical conductivity. Putting $\mu \sim 1$ and L a few hundred kilometres gives $1 < \delta < 50 \ (\Omega \ cm)^{-1}$ which, using Dyal and Parkin's data for basalt[18], indicates that the temperature of the liquid gabbro had to be not less than 1,900 K for the convective mechanism and not less than 1,600 K for the tidal mechanism. For the Apollo 11 sample[19] the corresponding minimum temperatures are 1,750 and 1,300 K. Thus the tidal mechanism seems to pose less stringent requirements for the generation of a magnetic field in the liquid shell than thermal convection. On the other hand, a more detailed quantitative evaluation of the history of the transient melting might alter this conclusion.

The strength of the magnetic field H produced in this way depends, of course, upon the actual configuration and topology of the currents and is very difficult to estimate. Recent studies[20] indicate that the generation of magnetic fields in rotating bodies is closely related to the presence of non-reflexion-symmetric turbulence such as one would expect to exist in tidal motions. By comparing the Coriolis and perturbing forces with the Lorentz force per unit mass $|(4\pi\rho)^{-1} \ (\nabla \times H) \cdot H|$ where ρ is the density of the liquid[6] one obtains, for currents with an effective radius of curvature of the order of kilometres, local fields of 10 gauss or more, which is very high. Clearly, for realistic and complicated boundary conditions, somewhat resembling those for tides in Earth's oceans, the local velocities and the local magnetic fields could be appreciably lower.

This admittedly very simplified model leads to the conclusion that the outer layer of the Moon could have been magnetized by local, more or less randomly oriented, magnetic fields produced by tidal currents, that there would be no overall poloidal field and that the magnetization would be observable primarily near the lunar equator where, from equation (1), the tide producing force has its maximum. All these conclusions seem to be in accord with the observations mentioned earlier and also the conflict with the stability requirements of the Moon is avoided. A detailed quantitative analysis of the tidal motions for a less idealized distribution of the liquid phase should be made. Such a distribution could be perhaps deduced from the most recent surveys of chemistry and morphology of lunar rocks and from the configuration of the surface magnetization and of surface fields.

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Rate of Horizontal Fault Displacement in New Zealand

WELLMAN[1] has estimated horizontal faulting rates in New Zealand. His presentation, however, takes little heed of published data relevant to recent crustal movements in New Zealand and his inferences are extremely tenuous.

Wellman states: "From seafloor spreading . . . the rate [of horizontal displacement] is estimated to be about 34 mm per year" and quoted Christoffel[2] and Wellman[3] in support. Christoffel, however, estimated "relative average rate of movement between 4.2 and 5.8 cm a year". The estimate of 34 mm per year is Wellman's alone.

In estimating an age of 10,000 yr for the Waiohine and other aggradation surfaces Wellman ignored the radiocarbon dates from which the dating of correlative aggradation surfaces in the South Island has been developed. These dates[4,5] indicate an age of about 18,000 yr for the latest principal aggradational surfaces developed during the latest (Otira) glaciation.

Wellman stated that at Turakirae Head "the highest [beach] ridge seems to be roughly 6,300 yr old. Radiocarbon dating of samples from beds a few metres below the highest beach ridge supports this estimate". In fact the radiocarbon dates referred to[6] are from a different section on a different structure 70 km away across the regional strike of several important structures, and the dating of the beach ridge depends on complex relations of tectonism and sea level rise[7].

We are unaware of the evidence on which Wellman bases the active dextral fault shown offshore off the southeast of the North Island; this was first postulated in 1971 by Wellman[8] without any substantiation. Later[3] in 1971 he merely noted that it was "reasonably well-defined by bathymetry to the northeast".

Wellman's assumption of a constant average rate of vertical movement ignores the evidence[9] of decreasing rate and reversals of vertical movements at many active faults since the formation of the last main aggradational surface. This makes calculations based on rates of vertical movement suspect. Wellman has to assume a changing average rate of horizontal movement at Waiohine rather than the constant rate for transcurrent faults in general that he has accepted previously[10,11].

The Cape Turakirae beaches lie on the anticlinal fold between the Wellington and Wairarapa Faults. Uplift there will result whenever accumulated strain along the fold is relieved by triggering from earthquakes associated with movement at any of the major faults in the region, not only at the Wairarapa fault, which displaces the Waiohine terraces. Uplift at Turakirae may thus be significantly more frequent than movement on the Wairarapa Fault at the Waiohine terraces. Wellman's inference that the same earthquakes caused movement in both places is not valid.

Wellman's ratio will remain the same if a constant factor exists relating frequency of uplift at Turakirae to faulting at Waiohine. No inference of age of the Waiohine surface and by extension of the rate of horizontal movement is possible without knowledge of such a factor. The Waiohine surface could well be several times older than Wellman assumes.

If one were to accept Wellman's 240 m summation of post-aggradation movement at the major faults, and an age of 18,000 yr for the latest principal aggradation surface, the rate of strain would be 13 mm yr^{-1}. This is little more than one-third of Wellman's estimate of 34 mm yr^{-1} and an even smaller part of either of Christoffel's estimates, all from seafloor spreading. Conversely, for Wellman's rate of 34 mm yr^{-1} the principal aggradation surfaces must be 7,000 yr old, which is unrealistic.

Suggate[12] has maintained and Freund[13] has accepted that there is no good evidence of large horizontal displacements in post-glacial time along the central section of the Alpine Fault, where Wellman's reconstruction would require the rate of strain (34 mm yr^{-1}) to be the sum of the rates on the faults of the shear belt to the northeast. Freund[13] has put forward

one possible hypothesis whereby the horizontal movement on these faults need not be transmitted to the Alpine Fault.

We urge those dependent on published literature for their knowledge of Recent crustal movements in New Zealand to study that literature as fully as possible. New Zealand's key position in relation to floor spreading makes such a study necessary.

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Magnetism and Archaeology

A RECENT discussion about reversed geomagnetic events in the Brunhes epoch contains the statement that no archaeological materials are known to be reversely magnetized[1]. This may be true for the specific region that is considered in the article, but it is not true in general. G. Folgheraiter in "Rendi Conti dei Licei", 1896, 1899; *Archives des sciences physiques et naturellas* (Geneva), 1899; *Journal de physique*, 1899; and P. L. Mercanton, in "La methode de Folgheraiter et son role en geophysique", *Archives des sciences physiques et naturellas*, 1907, reported observations made on clay fired in kilns by the Etruscans and Greeks. Their results indicate that in the eighth century BC the Earth's magnetic field was reversed.

In 1896 Giuseppe Folgheraiter made studies of Attic (Greek) and Etruscan vases of various centuries, starting with the eighth century BC. The observations were made on clay fired in kilns. The position of the ancient vases during firing is known. They were fired in a standing position, as indicated by the flow of the glaze. The magnetic inclination or the magnetic dip of the iron particles in the fired clay indicates the nearest pole during time of firing. His conclusion was that in the eighth century BC the Earth's magnetic field was reversed at least in Italy and Greece.

P. L. Mercanton of Geneva, studying the pots of the Hallstatt age from Bavaria (about 1000 BC) and from the Bronze Age caves in the region of Lake Neuchâtel, came to the conclusion that about the tenth century BC the direction of the magnetic field differed only slightly from its present direction. His material was of an earlier date than that used by Folgheraiter but, checking on the method and results of Folgheraiter, Mercanton found them correct[2].

This work has been brought to the attention of Elizabeth K. Ralph, Associate Director, the University of Pennsylvania Museum, who is presently investigating magnetic field reversals. She is considering investigation of material taken from kilns dating around the eighth century BC. These kilns were recently unearthed in Sarepta by James B. Pritchard who is also asso-

ciated with the museum. This work could provide additional valuable data in the investigation of magnetic field reversals.

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BIOLOGICAL SCIENCES

Metabolic Availability of Vitamin C in the Guinea-pig

THE results of studies in which L-gulonolactone-1-^{14}C, the precursor of L-ascorbic acid in the rat, was administered to guinea-pigs showed that the guinea-pig is apparently unable to synthesize vitamin C[1-3]. This has been attributed to the absence of gulonolactone oxidase from the liver microsomes of the guinea-pig; because this enzyme is the last one in the series for converting glucose to ascorbic acid it completely blocks endogenous synthesis. Synthesis of ascorbic acid has been demonstrated in rats: gulonolactone oxidase is present in their livers[4-6]. A defect, probably a conditional lethal mutation[7], in the gene controlling the synthesis of this enzyme in guinea-pigs produces an inactive enzyme or its complete absence. They are therefore dependent on exogenous vitamin C. This genetic disease has been named hypoascorbemia because of the low levels of ascorbic acid in the blood which are pathognomonic of the condition[8]. Neither the sex nor the age of the animals in these experiments was stated, and there was no indication of the state of ascorbic acid tissue saturation or of the scorbutic condition of the guinea-pigs.

Diet, age and sex greatly influence the metabolism of ascorbic acid in rats[9-12]. In spite of the evidence for the uniform presence of a conditional lethal genetic defect in guinea-pigs, Williams and Deason[13] demonstrated great variability in guinea-pig requirements for exogenous vitamin C in order to prevent the development of scurvy. Guinea-pigs do not develop scurvy on account of an excessively high rate of destruction of L-ascorbic acid[14], so it seems that some guinea-pigs have greater ability to synthesize ascorbic acid than others. The evidence of Burns[15] suggests that these guinea-pigs must have higher concentrations of gulonolactone oxidase in their livers, because their genetic defect is not as dominant as in the other less well-endowed members of the species[16]. Stone[16] has suggested that the extent of this defect could be determined by observing the development of scorbutic symptoms and measuring the ability of the guinea-pig to synthesize ascorbic acid while on a diet deficient in ascorbic acid. The results of such an investigation in the guinea-pig are described here.

Duncan-Hartley guinea-pigs, initially weighing 380–400 g, were used. They were housed singly and maintained on a normal diet of rabbit pellets containing 27 mg ascorbic acid/ 100 g pellets, and free access to water, of which each animal drank about 30 ml. daily. After 2 weeks of acclimatization to the diet and checking to exclude individual pathology, they were transferred to the scorbutogenic diet as described by Hughes and Hurley[17]; this contained ground oats, wheat bran, and skimmed milk, modified only by the addition of 0.5% instead of 1.0% supplementary vitamins and salts, excluding ascorbic acid. No vitamin C could be detected in this diet by chemical analysis. On transfer to the diet, supplementary ascorbic acid (50 mg 100 ml.$^{-1}$) was added to the drinking water so that each animal received about 15 mg supplementary vitamin C daily. This treatment was maintained for a further 2
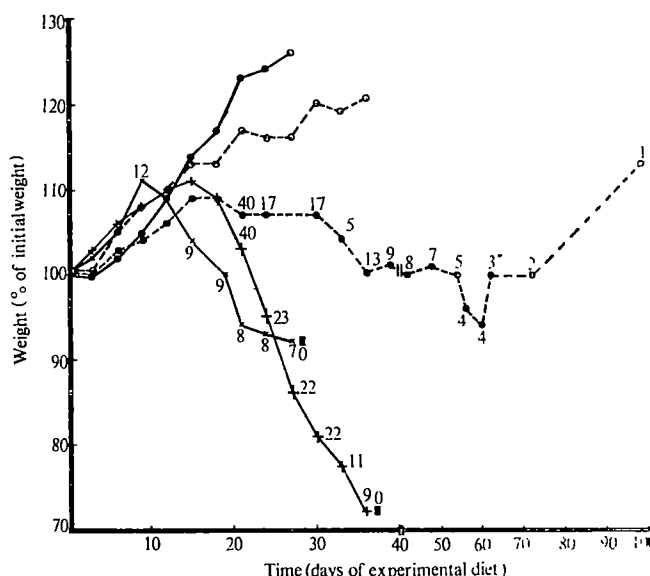
Fig. 1 Effect of ascorbic acid supplementation and deficiency on guinea-pig growth and survival. Survival times and alteration in weight of guinea-pigs maintained on a diet free of ascorbic acid. ⊙ – – – ⊙, Control females, diet + 15 mg ascorbic acid daily intraperitoneally. O——O, Males and females, diet + supplementary ascorbic acid 100 mg daily by stomach tube. ×——×, Male guinea-pigs, diet alone. ● . . . ●, Female guinea-pigs, Survivors, diet alone. +—+, Female guinea-pigs, Diers, diet alone. ■, 100% fatality. The numbers of guinea-pigs at each point of time in the males on diet alone, the female Survivors and the female Diers, are indicated.

weeks after which animals failing to maintain a steady growth pattern or showing impaired health were discarded. Following this 4 week maintenance period, a control group of females continued treatment with the scorbutic diet and 15 mg of supplementary ascorbic acid was given daily by intraperitoneal injection; a supplemented group, comprising equal numbers of males and females, received the diet together with 100 mg ascorbic acid given daily to individual animals by stomach tube; and separate groups of male and female guinea-pigs continued to receive the diet without any supplementary vitamin C (scorbutic groups). The animals were weighed every 3 days at 1000 h to avoid variations introduced by circadian rhythms. They were divided randomly into groups of six animals so that the killing order for tissue analysis was predetermined during the early part of the experiment. Guinea-pigs were killed at 1200 h by exsanguination after stunning. Ascorbic acid was measured, after extraction in 10% metaphosphoric-acetic acid mixture, by the phenyl hydrazine method[18-20]. Gulonolactone oxidase activity was detected in liver by a specific histochemical procedure using nitro-blue tetrazolium (Nitro BT), phenazine methosulphate, and potassium cyanide in the presence of L-1,4-gulonolactone[21].

In Fig. 1 the changes in body weight of male and female guinea-pigs on the scorbutogenic diet are compared with the weight changes in the control group of female guinea-pigs receiving the scorbutogenic diet and 15 mg of vitamin C daily by intraperitoneal injection, and with the gain in body weight of the supplemented group receiving the diet with 100 mg ascorbic acid administered daily by stomach tube.

The control group gained weight steadily during the 36 days of the experiment. The supplemented group began to gain weight more rapidly than the control group after day 18. By day 24 the supplemented group was significantly heavier than the control group. Two separate experiments were carried out on male scorbutic groups. In the first experiment, they became slightly heavier than the control or supplemented groups during the first 12 days of the experiment, then quickly lost weight. They had lost all their additional weight by day 24. On day 27

their weight was less than at the beginning of the experiment, they showed scorbutic signs and were dying spontaneously. In the second experiment, two out of six animals were dead, two were moribund, and two were showing severe scorbutic signs and died on day 30. The mean liver and plasma ascorbic acid concentrations of the latter four animals were 1.06 ± 0.21 mg per 100 g and 0.055 ± 0.001 mg per 100 ml. respectively. Two separate experiments were also performed on the female scorbutic groups. Fifty-four animals started the scorbutogenic diet in the first experiment. Their record of survival has already been described[22]. Thirty-six received the diet in the second experiment and these animals either died, were deliberately killed as required for tissue analysis, or were subjected to special tests during the experiment. On day 72 two were still alive and gaining weight. The final survivor died on day 154 from infection following a series of vaginal examinations. The results are summarized in Fig. 1 and Table 1.

Table 1 Mean Ascorbic Acid Concentrations in the Livers (mg per 100 g) and Plasma (mg per 100 ml.) of Guinea-pigs Maintained on an Ascorbic Acid Free Diet

Day of diet	Males No.	Liver	Plasma	Female Survivors No.	Liver	Plasma	Female Diers No.	Liver	Plasma
0	6	27.48	0.43	6	20.42	0.88			
6	6	24.35	0.50	6	16.35	1.03			
12	6	16.08	0.37	6	7.17	1.02			
18	6	6.29	0.21	6	2.25	0.46			
24				3	2.08	0.25			
27	2	0.30	0.09						
30	4	1.06	0.06				11	2.16	0.12
32				2	3.90	0.17			
35				1	4.27	0.20			
36				3	5.64	0.22	6	2.97	0.08
62				1	4.69	0.57			
72				1	8.17	0.18			
98				1	11.04	1.40			

On day 24, the females were differentiated into potential Diers and potential Survivors on the basis of their growth patterns.

During the first 15 days, the scorbutic females gained weight almost as rapidly as the control and supplemented groups. By day 18 the scorbutic group had begun to lose weight. On day 24 they were significantly lighter than the female control group as has also been reported by Hodges and Hotston[23]. The guinea-pigs in these investigations, however, did not receive ascorbic acid supplementation before the experiment, thus accounting for the appearance of a moribund condition by day 24. At this time scorbutic females could be divided into two groups, the potential Diers and the potential Survivors, on the basis of their growth patterns. From day 24 until the end of the experiment, the Diers showed a rapid and steady decrease in weight. On day 24 they were showing scorbutic symptoms. They all died during the first 36 days of the diet. The Survivors ceased to gain weight after day 18. They showed a gradual stepwise decline in weight until day 36 when their weight had fallen to the level at the beginning of the experiment. They maintained this initial weight, apart from a temporary relapse on day 60, until day 72 of the scorbutic diet after which the surviving guinea-pigs gained weight steadily and uniformly. Retrospective analysis of the weights of the Diers and Survivors before day 24 demonstrated that the Diers initially gained weight more rapidly than the Survivors. After day 24, the Diers lost weight much more rapidly than the Survivors. When any of the surviving female guinea-pigs died, they did not show severe scorbutic signs like those of the males or female Diers.

Food intake of males and females rose until day 12. On day 24 it had returned to its original level in the females, but it continued to fall in the males and was 57% of normal when they were dying. From day 27 until day 72 it remained at 70% of the original level in the surviving females. At the end of the

experiment the surviving females were consuming 82% of the initial group food intake.

Plasma and liver ascorbic acid concentrations were measured in males and in female Survivors and Diers as the experiment proceeded (Table 1). Those killed among the Diers were generally moribund at the time of death. Animals selected for tissue analysis among the Survivors had the lowest body weights. The numbers on each occasion were determined by the total number available in the group. Liver ascorbic acid values diminished in both sexes during the first month. The rate of fall was greater in the females. Liver ascorbic acid reached its minimum on day 24 when it was 10.6% of the initial value. The maximal rate of fall was later in the males, and took place when the decrease in body weight was most pronounced. On day 27 the liver ascorbic acid was 1% of the initial value in the males. After day 24 the mean liver ascorbic acid concentrations ceased to fall in the female Survivors. Ascorbic acid was present in relatively high concentration in the livers of the Survivors killed on days 72 and 98. On day 98 the liver ascorbic acid value was 54% of that in the normal animals killed before the diet was started.

Plasma ascorbic acid levels were elevated in both sexes at the beginning of the scorbutogenic diet but the elevation was maintained for 6 days longer in the females. They had reached a minimum in both males and females on day 30. The mean ascorbic acid concentration had begun to rise in the female survivors on day 32. Plasma levels were still diminishing in the Diers even though liver concentration had begun to rise slightly. When the diet was started, liver values began to fall while plasma levels were elevated. Subsequently the rise in plasma ascorbic acid only occurred after raised levels had been detected in the liver.

Table 2 Mean Weights of Surviving Guinea-pigs Maintained on Scorbutogenic Diet Alone, and the Effect of PCMB, 0.3 mg IMI on their Weights while Maintained on the Diet Alone or on the Diet Supplemented with Ascorbic Acid (15 mg Daily)

Type of treatment		No. of guinea-pigs	Days 0	1	4	8
Diet	PCMB		Mean weights (g)			
Scorb.	None	3	435	462	472	478
Scorb. + Suppl.	Daily	2	515	526	534	543
Scorb.	Daily	2	444	482	466	355

Day 1 corresponds to day 54 of the scorbutic diet and to day 4 of the supplemented diet.

Raised ascorbic acid concentrations in the liver before any change in plasma levels suggested that ascorbic acid originated in the liver. Staining of the liver of male and female rats with Nitro BT demonstrated the presence of gulonolactone oxidase. Similar and simultaneous treatment of the liver of the female guinea-pig maintained on the scorbutogenic diet for 98 days demonstrated the presence of brown granules within the hepatic centrilobular cells. The brown granules in the guinea-pig liver were identical in distribution and appearance to those demonstrated in rat liver after staining with Nitro BT. Similar brown granules were not visible in the liver of a male guinea-pig supplemented with ascorbic acid. They could not be detected along the centrilobular cell boundaries in the liver of a male guinea-pig killed on day 28 of the scorbutogenic diet although scanty deeper staining was occasionally visible in the peripheral zone.

It has been demonstrated by chemical methods that the rate of conversion of L-gulonolactone into L-ascorbic acid is strongly inhibited by p-chloromecuribenzoate (PCMB), and that this effect is caused by the inhibition of thiol groups in the enzyme gulonolactone oxidase[3]. The inhibitory effect of PCMB on gulonolactone oxidase has been confirmed by histo-

chemical studies[21]; pretreatment with PCMB of animals known to have gulonolactone oxidase in their livers eliminated detection of the hepatic enzyme by means of its staining properties. In our investigations two of the surviving guinea-pigs were withdrawn from the experiment on day 54 and treated with PCMB, which resulted in significant loss of weight and death on day 62, 8 days after the beginning of treatment. Three other Survivors in the same group of guinea-pigs uniformly gained weight during this period. Two control guinea-pigs receiving the scorbutogenic diet supplemented with 50 mg ascorbic acid daily in their drinking water, and also treated with PCMB, gained weight during the 8-day period in the normal fashion (Table 2). The effect of gulonolactone supplementation of male and female guinea-pigs on the scorbutogenic diet has been described by Odumosu and Wilson[24]. The daily administration of 30 mg kg^{-1} of gulonolactone more than doubled life expectancy in male guinea-pigs on the diet and prolonged it in females which lived longer on average than the males. This suggests that early and continuing activation of gulonolactone oxidase (which is essential for the synthesis of ascorbic acid in several other species[21,25]) in the presence of adequate gulonolactone is necessary, in female guinea-pigs, for prolonged survival in the absence of exogenous vitamin C.

Ascorbic acid is released from the labile stores in the buffy coat of the blood into the plasma[26] accounting for the initial increase in the amount of plasma ascorbic acid. It is removed from the plasma by the tissues, such as the adrenal gland, for whose continued metabolic activity it is essential. The liver requires ascorbic acid for its metabolic activity[27], and the concentration in the liver consequently falls as soon as the exogenous supply is stopped. After day 24 of the diet, liver synthesis of ascorbic acid rises to a level sufficient to maintain the hepatic metabolic requirements, but plasma levels continue to fall. By day 35, some escapes into the plasma from whence it is absorbed by other tissues. Female guinea-pigs in which the body weight does not fall below the initial value within the first 24 days of the diet seem to be potentially capable of synthesizing ascorbic acid. If they maintain a weight within 10% of the initial value up to the 60th day of the diet they will survive for a variable period. After day 92, body weight steadily increases in the same way as in control animals not subjected to the scorbutogenic diet. Animals showing a rapid loss of body weight after day 24 of the diet, and a subsequent decrease to below the initial weight, are potential Diers unable to synthesize sufficient ascorbic acid to satisfy essential body requirements. These animals develop scorbutic symptoms and the liver becomes pale and greasy. Deficiency of ascorbic acid impairs fat metabolism[28]. The alterations in weight, and associated morphological changes in the liver, are among the earliest signs of uncompensated ascorbic acid deficiency in the guinea-pig[22].

Release of repression of the gene, controlling the ability to synthesize ascorbic acid, may occur in some female guinea-pigs by virtue of the fact that the enzyme can be activated when there is a deficiency of exogenous vitamin C. This activation seems to occur predominantly in female guinea-pigs. The rate and maintenance of enzyme activation also determine whether enough ascorbic acid can be manufactured to enable tissues to maintain their vital metabolic functions and thus prevent otherwise inevitable death from scurvy. Variations in requirements for ascorbic acid, demonstrated by the presence of circadian and monthly rhythms[29-31] and by variations in ascorbic acid requirements in relation to cortisol secretion[18], are associated with considerable alterations in metabolic demand for ascorbic acid on a temporal and on a tissue basis. The combined operation of the genetic, circadian and stress factors in guinea-pigs is adequate to explain the individual variation in the requirements for ascorbic acid and development of scorbutic signs, which was reported by Williams and Deason[13].

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Dietary Cholesterol, Sex and Scurvy in Guinea-pigs

THERE is evidence that in man the vitamin C (L-xyloascorbic acid, AA) concentration in both the plasma and leucocytes is higher in females than in males[1,2]. On the other hand, studies with guinea-pigs receiving a controlled daily intake of AA revealed no significant sex difference between the AA concentrations in the adrenals, spleen and brain, and in the eye lens the AA concentration was significantly lower in females than in males[3].

Odumosu and Wilson have recently claimed that "in times of stress, some female guinea-pigs are able to readjust their ascorbic acid metabolism and so compensate for the influence of the defective gene responsible for hypoascorbemia"[4]. Their results indicated that some female guinea-pigs could survive for up to 60 days on a scorbutogenic diet. This is in con-

trast with the generally accepted survival period of 20–30 days for male guinea-pigs given a scorbutogenic diet and would be unexpected in the light of the absence of any significant sex difference in the rates of loss of AA from the organs of guinea-pigs deprived of dietary AA[5].

The experiment described in this note was designed further to examine the influence of sex on the survival of guinea-pigs given a scorbutogenic diet. The influence of a diet with a high cholesterol content was also examined. This was done because of recent indications of a possible metabolic relationship between AA and cholesterol[6,7]; if AA plays an essential part in the metabolism of cholesterol then loading the body with cholesterol would be expected to shorten the survival time of guinea-pigs given a scorbutogenic diet.

Albino guinea-pigs (Dunkin-Hartley 'Pirbright' strain) of initial body weight 300–350 g were used and housed and fed as previously described[8]. The diet had the following composition: ground oats 37 g, wheat bran 35 g, dried skim milk (1% fat) 20 g, dried yeast 6.5 g, salt mixture (Glaxo Research Ltd) 1.0 g, magnesium oxide 0.5 g. Previous work had shown that male guinea-pigs given this diet without AA developed scurvy and died within 24–27 days; when supplemented with AA, normal growth was maintained[9].

Table 1 Tissue Concentrations of Ascorbic Acid (AA) at Start of Depletion Period (after 12 Days Supplementation with AA)

| | Ascorbic acid (mg 100 g^{-1}) | | |
	Adrenals	Spleen	Brain
Males	214.8 ± 11.1	55.3 ± 1.7	24.6 ± 0.5
Females	226.9 ± 8.3	55.3 ± 2.1	25.6 ± 0.4

Each value is the mean with s.e. for four animals.

Thirty males and thirty females were used. All animals received 1% AA in the drinking water for 12 days immediately prior to the depletion period to produce similar saturation levels of tissue AA. On day 13 of the experimental period (= day 1 of the depletion period) four animals from each group were killed and their tissue AA levels determined (Table 1). The remaining twenty-six animals in each sex group were randomly assigned to two sub-groups of thirteen, one of which received the standard diet and the other the standard diet plus 0.3% cholesterol. The survival periods were measured (Table 2).

Table 2 Deaths of Male and Female Guinea-pigs given Scorbutogenic Diets with High or Low Cholesterol Content

Survival period (days)	High cholesterol diet Male	High cholesterol diet Female	Low cholesterol diet Male	Low cholesterol diet Female
9	0	0	1	0
15	0	0	0	2
17	1	0	0	0
24	0	0	0	1
25	0	2	2	2
26	2	1	0	1
27	4	1	3	2
28	1	3	3	2
29	4	3	1	0
30	1	1	2	0
31	—	1	0	3
32	—	1	1	—
Mean survival time (d) with s.e.	27.0 ± 0.8	28.2 ± 0.5	26.5 ± 1.5	25.6 + 1.4
	(27.8)	(28.2)	(28.0)	(27.5)

The values in parentheses are for the deaths occurring after day 20; guinea-pigs rarely die from scurvy in less than 20 days and the deaths on days 9, 15 and 17 could well have occurred from other causes.

The male and female animals had similar tissue AA concentrations at the commencement of the depletion period (Table 1) and there was no significant sex difference between the

mean survival times (Table 2). Furthermore, the additional stress introduced by the presence of cholesterol had no apparent influence on survival time. This experiment therefore does not support the claim that female guinea-pigs are less susceptible to scurvy than are males; nor does it provide evidence that there is an essential involvement of AA in the metabolism of exogenously-introduced cholesterol (although large doses of AA may nevertheless influence the metabolism of cholesterol). It may be noted that a recent population survey failed to produce any evidence of a correlation between blood AA and plasma cholesterol[10].

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Mortality Rate in Male and Female Guinea-pigs on a Scorbutogenic Diet

Odumosu and Wilson[1] have reported the unexpected observation that a significant proportion of female guinea-pigs were able to survive for an unusually long period (in some cases perhaps indefinitely) on a diet free of ascorbic acid, implying that these animals could synthesize the vitamin endogenously. The literature on experimental scurvy in guinea-pigs contains, as far as we are aware, no past studies on the mortality of guinea-pigs deprived of an exogenous source of ascorbic acid in relation to sex. In experiments the animals were killed before they reached the point where death from scurvy might be expected, and the sex of animals was either not stated or male only. Nevertheless it has been assumed that both male and female guinea-pigs require an exogenous supply of ascorbic acid and that administration of an ascorbic acid-free diet would lead to the death of all animals, irrespective of sex, within 3–4 weeks. In view of the importance of the observation of Odumosu and Wilson[1] in respect of the nature of the lesion in ascorbic acid metabolism in guinea-pigs and as it might reflect on the requirements of humans for an exogenous supply of the vitamin, we felt it necessary to verify their finding.

An ascorbic acid-free diet similar to that described by Reid and Briggs[2], and full details of which are given below, has been in use in this laboratory for some years. This diet invariably produces, at least in male guinea-pigs, a rapid depletion of tissue ascorbic acid and a loss of appetite which

leads to a reduced food intake and fall in body weight beginning around 10 days of ascorbic acid deprivation. Characteristically, the animals exhibit a marked lassitude, poor coat condition and stiffness in the joints; they seem reluctant to place any weight on their limbs and come to adopt a typical scorbutic posture. Death generally follows 3-4 weeks after introduction of the ascorbic acid-free diet[3].

For this experiment we used young albino guinea-pigs (Frant strain obtained from Mr T. Cowen, Bartlow Farm, Bartlow, Cambs., an experimental station attached to this laboratory), of both sexes. The basal, ascorbic acid-free diet used had the following composition, in parts by weight: sucrose, 103; glucose, 78; salt mixture (described below), 60; maize starch, 200; potassium acetate, 25; maize oil, 73; casein, 300; cellophane, 150; choline chloride, 2, and vitamin mixture (see below), 7.3. The salt mixture had the following composition in g kg^{-1}: calcium carbonate, 205; calcium hydrogen phosphate, 325; disodium hydrogen phosphate, 185; potassium chloride, 205; magnesium sulphate, 70; manganese sulphate, 4.5; ferric citrate, 4.35; copper sulphate, 0.375; zinc carbonate, 0.75; and potassium iodate, 0.025. The vitamin mixture consisted of the following in the proportions indicated: thiamine hydrochloride, 16 mg; riboflavin, 16 mg; pyridoxine hydrochloride, 16 mg; calcium d-pantothenate, 40 mg; cytamin, 0.05 mg; nicotinamide, 200 mg; folic acid, 10 mg; biotin, 1.2 mg; magnesium oxide, 5 g; inositol, 2 g; and 'Rovimix E' (equivalent to 250 mg α-tocopheryl acetate/g), 200 mg. Control animals received the basal diet supplemented with ascorbic acid at 2 g kg^{-1} of diet. All animals had free access to food and water. Each animal also received by mouth, once a week, 344 μg retinyl acetate, 5 μg ergocalciferol, 2 mg α-tocopheryl acetate and 50 μg 2-methyl-1:4-naphthoquinone (all dissolved in arachis oil).

All animals initially received the ascorbic acid-supplemented diet for a 2-week period of acclimatization. Animals of satisfactory growth rate were then divided as follows: a total of thirty-four male and thirty-five female animals were placed on the ascorbic acid-free diet; six male and seven female control animals continued on the ascorbic acid-supplemented diet.

Table 1 Survival Time in Male and Female Guinea-pigs Fed an Ascorbic Acid-free Diet

Survival time (days)	No. of guinea-pigs Male	Female
16	0	1
17	0	0
18	0	1
19	0	4
20	1	0
21	8	5
22	6	4
23	7	3
24	3	8
25	2	6
26	2	1
27	2	1
28	2	0
29	1	1
Total	34	35

The mean survival time for both male and female groups was 23 days.

All control animals continued to gain weight throughout the experimental period. Animals fed the ascorbic acid-free diet, however, began to lose weight on average after 10 days of vitamin deprivation in the male group and

after nine days in the female group. Concomitantly, these animals began to assume the typical scorbutic appearance as described earlier. Loss of weight continued until the death of the animal. Mean weight at the start of the experiment was 244 g for the male and 242 g for the female group on the ascorbic acid-free diet; mean weight at death was 170 g for the males and 165 g for the females. As shown in Table 1, the mean survival time was 23 days in each case. At this time control animals (all of which survived) weighed around 300 g (from a mean starting weight for male and female together of 224 g). None of the animals fed the ascorbic acid-free diet survived beyond 29 days on this diet. These data concur with similar data obtained independently by Dr R. E. Hughes and his colleagues[4].

The reason for the prolonged survival of some female guinea-pigs in the study of Odumosu and Wilson[1] in contrast to the 100% mortality within 3-4 weeks in our study and that of Jones, Hurley and Hughes[4] is not clear. Odumosu and Wilson[1] indicate that seventeen from a total of forty female guinea-pigs could be differentiated as "potential survivors" on an ascorbic acid-free diet. Details of this diet are not provided. Conceivably it may have contained traces of ascorbic acid. If this were so, it might be possible to argue that female guinea-pigs are more adept than males in absorbing and retaining the vitamin when it is available in trace amounts only. In any case our results do not support the contention that some females can synthesize the vitamin in response to a complete absence of an exogenous source.

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Rapid Generation of Whole-Body Radioautograms with Microchannel Plate Electron Image Amplifiers

WHOLE-BODY radioautography is a useful method for studying the distribution of radio-labelled compounds among all the organs and tissues of an experimental animal[1-4]. Rapid excretion of radio-labelled drug, low energy radiation as in tritium, or low specific activity of isotopes often require weeks or months of exposure of emulsion to whole-body sections for the generation of radioautographic data. Here we describe a new simple technique for efficient, rapid generation of radioautographic images, using a microchannel plate electron image amplifier to detect electrons emitted from the surface of labelled tissue.

The microchannel plate[5,6] (Bendix Research Laboratories) is a small, simple low-noise amplifier of electron images (Fig. 1). Each of a parallel array of glass tubes is coated on the inside with a material which conducts electricity and also emits multiple electrons upon a single electron impact. About
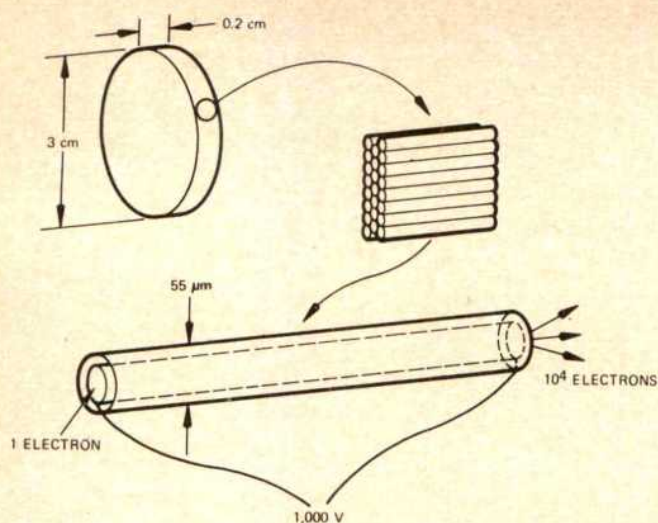
Fig. 1 Microchannel plate.

1,000 V are applied across the channel plate, and the electron gain is about 10^4.

Specimens were placed against the input surface of the microchannel plate in a high vacuum chamber (10^{-6} Torr); vacuum was produced with an oil diffusion pump (Fig. 2). As tritium decays, electrons emerging from one tissue surface are multiplied in the active volume of a microchannel plate (MCP) and give rise to a several-thousand-fold electron emission, which is imaged onto a phosphor screen, light from which is photographed by a camera. The image quality is limited by resolution of the MCP, the noise level of the MCP amplifier, and the number of beta-particles per unit of image resolution; in our experiments a useful image was acquired in 15 min (Fig. 3B).

Thirty minutes after i.v. dosage with tritiated deoxycycline (Pfizer, 4.4 mg kg⁻¹, 5.5 mCi kg⁻¹), 50 g rats were frozen in hexane-CO_2 and whole-body sections were prepared. A whole-body section, one inch in diameter, was placed against the microchannel plate, and about 1,000 disintegrations/min were estimated in this area. The phosphor screen was photographed with 'Polaroid 57' film. Exposure times ranging from 15 to 30 min were sufficient to record enough tritium disintegrations to generate a useful image.

Fig. 3A shows the area of a whole-body section which was assayed with the microchannel plate. The corresponding MCP radioautographic image is seen in Fig. 3B. A conventional radioautogram which was generated by exposing 'Kodak No-Screen' medical X-ray film to an adjacent whole-body section for 10 weeks is seen in Fig. 3C. A disadvantage of our technique is that the microchannel plate-derived image (MCPI) is limited by the statistics of tritium decay[7-10] and exhibits inferior resolution ($n \sim 30$ μm) to that achieved by conventional radioautography ($n = 0.2$ μm).
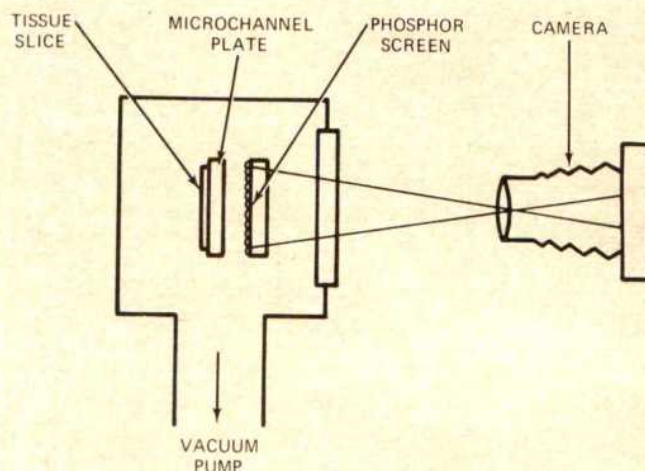
Fig. 2 Radioautography system.

In conclusion, the microchannel plate electron image amplifier has demonstrated a great advantage in speed compared with the conventional X-ray film radioautogram. The technique is simple and can be applied to whole-body sections, paper chromatograms, or any fixed solid material that can withstand high vacuum and that does not cause contamination of a vacuum system. With such samples, the microchannel plate and phosphor screen can be exposed to the atmosphere and used over and over again. With presently available components, images from a specimen up to 7.5 cm in diameter could be recorded with resolution of about 30 μm. Microchannel amplifiers with unit resolutions smaller than 10 μm are now
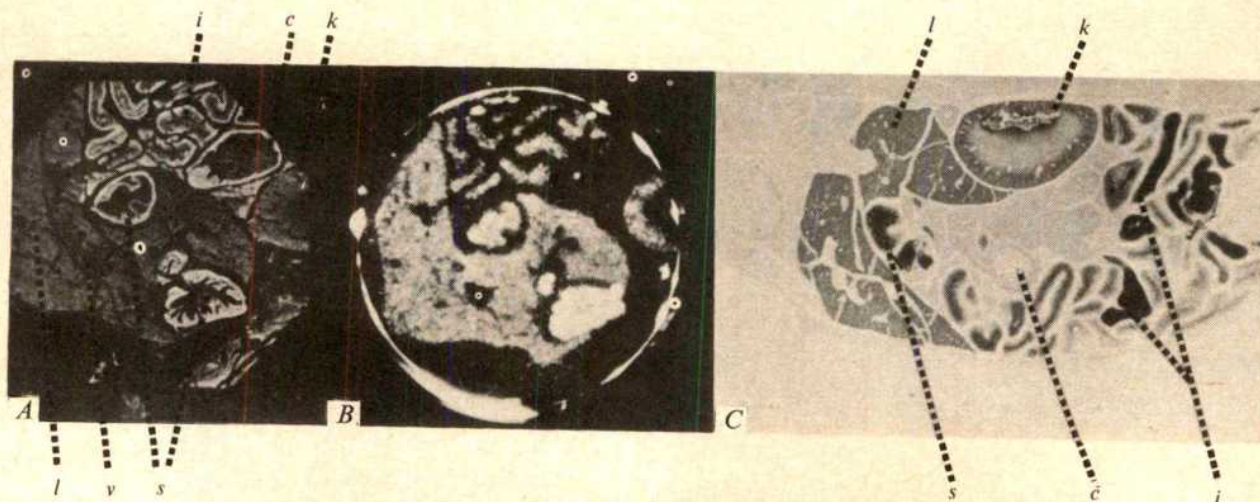
Fig. 3 *A*, Polaroid picture of the area of a whole-body section which was assayed with the microchannel plate. *c*, Colon; *i*, small intestines; *k*, kidney cortex; *l*, liver; *s*, stomach; *v*, hepatic vasculature. ×1.5. *B*, Polaroid picture of microchannel plate-derived radioautographic image of tissues in *A*. (Light areas correspond to tissue concentrations of drug-derived ³H.) ×1.5. *C*, Conventional radioautogram generated by exposing X-ray film to a whole-body section for 10 weeks. (Radioautogram density corresponds to tissue concentration of ³H.) ×1.5.

becoming available to the commercial market and may provide yet higher resolution of radioautograms.

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Inhibition of the Acute Inflammatory Response by Interferon Inhibitors

MEDIATORS responsible for the development of inflammatory reactions have been extensively studied. Much less is known about anti-inflammatory mechanisms. During the past 15 years evidence has accumulated that anti-inflammatory factors are released at the site of inflammation[1–10]. Research in this area has been stimulated by the introduction of the carrageenin foot oedema test[11], which is very sensitive to endogenous anti-inflammatory factors[7].

We observed that a synthetic polynucleotide, polyriboinosinic-polyribocytidylic acid (poly (I–C)), inhibited carrageenin and dextran-induced inflammation in the rat without influencing turpentine pleurisy (our unpublished results). Poly (I–C) has a stronger antiviral effect than is apparently accounted for by interferon production[12]. As there is growing evidence that interferon and its inducers have multiple effects, we decided to investigate whether interferon inducers are involved in controlling the acute inflammatory process, and whether any activity observed could be explained by interferon production.

We studied the effect of three interferon inducers, poly (I–C), double-stranded (DS) Statolon RNA[13] and Semliki Forest Virus (SFV), and that of a purified interferon preparation, on the acute inflammation induced in mice by carrageenin.

Six-week-old male CFLP mice weighing 20 ± 0.9 g were used. Carrageenin inflammation was induced according to the method of Levy[14]. For the evaluation of the inflammatory reaction, the differences between the weight of the saline and carrageenin-injected paws were expressed.

Interferon titres in mouse pooled sera were determined in tube cultures of mouse L cells using vesicular stomatitis virus (Indiana serotype). Poly (I–C) and poly (A–U), 18 Sw_{20} and 6 Sw_{20}, respectively, were the products of Reanal (Budapest, Hungary). Purified interferon was a gift from Dr G. Bodo, Arzneimittelforschungs-Institut (Vienna, Austria), and the DS RNA of Statolon was kindly supplied by Dr W. J. Kleinschmidt, Lilly Research Laboratories (Eli Lilly and Co., Indianapolis, Indiana).

Table 1 Effect of Poly (I–C), DS Statolon RNA and Poly (A–U) on Carrageenin-induced Acute Inflammatory Response and Interferon Production in Mice

Pretreatment		Dose (mg/kg)	Increase in weight of paws caused by carrageenin (mg ± s.d.)	Inhibition of inflammatory response (%)	P	Interferon titre (units)
Untreated	(15)	—	70.7 ± 10.43	—	—	0
Poly I–C	(10)*	0.04	59.2 ± 4.82	16	0.05	5
	(10)	0.4	48.7 ± 5.87	31	0.0025	200
	(10)	4.0	41.2 ± 7.97	42	0.0005	1,000
	(10)	40.0	20.0 ± 4.35	71	0.0005	3,060
Statolon	(6)‡	0.04	64.2 ± 8.56	9	NS	5
	(6)	0.4	51.0 ± 8.32	28	0.0025	100
	(10)	4.0	46.6 ± 8.33	34	0.0005	900
Poly A–U	(10)†	0.04	71.4 ± 9.75	0	NS	5
	(10)	0.4	68.8 ± 8.67	3	NS	20
	(10)	4.0	61.6 ± 6.58	13	NS	60

Number of CFLP mice given in parentheses. * Sw_{20} of poly (I–C) was 18; † Sw_{20} of poly (A–U) was 6; ‡ DS RNA of Statolon from mycophage of *P. chrysogenum*, Lot 354–1110B–62. NS, not significant. The materials were injected intraperitoneally 3 h before induction of carrageenin inflammation.

When the mice were treated with various doses of poly (I–C) and Statolon RNA 3 h before administration of carrageenin, considerable inhibition of the inflammatory response was observed (Table 1). The anti-inflammatory effect was dose-dependent and paralleled interferon production. There was no significant anti-inflammatory effect or interferon production, however, after treatment with poly (A–U). The kinetics of inhibition of acute inflammation and of interferon production were also determined (Table 2). When poly (I–C) was given simultaneously with carrageenin, the blocking effect was only moderate. If the polynucleotide was injected 1.5 or 3 h before carrageenin, however, a pronounced anti-inflammatory effect

Table 2 Inhibition of Carrageenin-induced Acute Inflammatory Response and Interferon Titres in Mice treated with Poly (I–C) and Infected with SFV

Pretreatment		Time (h)*	Increase in weight of paws caused by carrageenin (mg ± s.d.)	Inhibition of inflammatory response (%)	P	Interferon titre (units)
Untreated	(15)	—	71.3 ± 11.23	—	—	0
Poly (I–C)	(8)†	0	50.6 ± 6.02	29	0.0005	NT
	(8)	1.5	42.4 ± 4.58	40	0.0005	NT
	(11)	3	42.2 ± 7.97	41	0.0005	1,000
	(9)	12	43.6 ± 6.22	38	0.0005	1,000
	(9)	24	45.5 ± 14.72	34	0.005	640
	(8)	48	58.0 ± 10.6	19	0.025	5
Mouse brain suspension	(10)‡	6	69.2 ± 10.45	3	NS	NT
SFV	(15)§	6	48.5 ± 7.78	32	0.0005	1,600
	(12)	12	30.7 ± 6.54	57	0.0005	7,600
	(11)	24	35.6 ± 9.3	50	0.0005	1,920
	(8)	48	45.7 ± 12.27	36	0.005	240

Numbers of CFLP mice are in parentheses. * Time of administration of interferon inducers before carrageenin injection. † Poly (I–C) ($Sw_{20} = 18$) was injected intraperitoneally in a dose of 4.0 mg/kg⁻³. ‡ Normal brain tissue (2 mg) was suspended in 0.2 ml of 0.9% saline. § 5×10^8 plaque forming units per mouse in a suspension containing 2 mg of infected brain tissue in 0.2 ml of 0.9% saline. NT, not tested; NS, not significant. All the materials were injected intraperitoneally.

was observed. This suggests that a short period of time is required for the anti-inflammatory effect to reach its maximum, and it may, therefore, not be a direct effect of poly (I-C). The anti-inflammatory activity was long-lasting and correlated with the serum interferon titres. Ten days after adrenalectomy, the anti-inflammatory activity of poly (I-C) remained unchanged.

Infection with SFV also inhibited carrageenin-induced inflammation (Table 2). As the SFV was not highly purified, similarly prepared brain tissue of young uninfected mice was also tested and found to produce no inhibition of the inflammatory response. Six hours after infection with SFV the anti-inflammatory effect was not pronounced. Twelve and 24 h later the inhibition was strong, and the concentration of interferon in the serum was higher than in mice given poly (I-C) or double stranded Statolon RNA.

Mice were also treated with purified mouse (L cell) interferon. 100,000 plaque depressing units injected intravenously decreased oedema by only 24% (Table 3).

Table 3 Effect of Purified Interferon on Carrageenin-induced Inflammation in Mice

Group	Increase in weight of paws caused by carrageenin (mg ± s.d.)	Inhibition of inflammatory response (%)	P
Control (10)	73.0 ± 9.92	—	—
Interferon (10) *	54.0 ± 8.37	24	0.005

* The animals received 100,000 plaque depressing units of mouse L cell interferon (330,000 units mg^{-1} protein) intravenously per animal 1 h before the subplantar injection of carrageenin. Numbers of CFLP mice are in parentheses.

Our experiments indicate that in CFLP mice, poly (I-C) and double stranded Statolon RNA exert a marked anti-inflammatory effect when studied in the carrageenin foot oedema test. This effect appears to be a reliable indicator of the interferon inducing capacity of these agents. The experiments also show that in the initial hours of SFV infection there is minimal anti-inflammatory activity, although interferon concentrations are high. The absence of a strong anti-inflammatory effect with purified interferon suggests that factor(s) other than interferon might also play a role in this phenomenon.

Kapusta and Mendelson[15] reported that adjuvant arthritis was strongly suppressed by Statolon. They did not suggest that interferon was responsible for this effect, as turpentine-induced inflammation was not influenced. Our earlier (unpublished) results in rats also suggest that poly (I-C) inhibits carrageenin and dextran inflammation without influencing turpentine pleurisy. This may be due to the insensitivity of the turpentine-induced inflammatory response to endogenous anti-inflammatory products. The fact that the anti-inflammatory effect of poly (I-C) is unaffected by adrenalectomy indicates that glucocorticoids are not involved in the phenomenon.

In conclusion, our experiments suggest that, although interferon has some inhibitory effect on acute inflammation, interferon inducers are more pronounced in their anti-inflammatory activity. It will be important to determine whether the "trigger" for the anti-inflammatory effect is identical to or separate from the "trigger" for interferon production.

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Electrostatic Forces in Some Hapten-Antibody Reactions

THERE is considerable interest in explaining the high specificity characterizing many of the reactions between biomolecules, in terms of interaction forces[1-3].

One system which readily lends itself to this type of study is a series of cross-reactions of a series of related haptens with a given antibody. Using precipitation techniques, Pressman et al.[4,5] determined the relative free energies of binding for a series of substituted trimethylammonium ions with carboxylate-containing antibody sites and have estimated the distance of approach of the hapten to the carboxylate, on the basis of a model in which the full positive charge is placed on the central nitrogen. New and Richards[6] recognized the variability of ionic charge distributions, and tried to correlate the measured free energies of association and the charge density on the hapten nitrogens, computed by the EHT[7] molecular orbital method. As well as dangers of generalizing on the nature of this type of interaction on the basis of a series of only eight haptens, the claim of correlation seems somewhat questionable as three of the eight haptens are ordered incorrectly according to charge magnitudes. We therefore re-examined this, emphasizing two aspects of the problem of selective binding. First, we will demonstrate and explain the failure of the central nitrogen charge to account for the specificity. Second, and more important, we will attempt to determine whether the underlying cause of the specificity can be explained in terms of simple electrostatics at all.

The electrostatic interaction between a hapten and an antibody site can be calculated exactly, subject to the assumptions of a model for the site and the availability of wave functions for the interacting species. We assume, for simplicity, that the antibody reactive site on the hapten consists of a singly charged ionic group. We have calculated the IEHT[8] charge distributions for the series of haptens. The approximate nature of the wave functions does not detract from the generality of the present work, as we are interested in relative quantities. Our second approximation, that of "hard sphere" atoms approaching to Van der Waals's distances, neglects the calculation of short-range repulsive forces. As the groups in contact remain unchanged through the series, however, this repulsion will remain approximately constant, and is unlikely to affect the relative binding energies.

With these assumptions, the electrostatic potential energy interacting with the negative point charge at site a is

$$E = \Sigma_i Z_i/R_{ia} - \underset{\mu}{\Sigma}\ \underset{\nu}{\Sigma}\ P_{\mu\nu} \int \chi_\mu(1)\ \chi_\nu(1)/r_{1a}.d\tau_1 \qquad (1)$$

where $P_{\mu\nu}$ is the bond order matrix, χ is an element of the atomic orbital basis and Z_i is the nuclear charge on centre i. All two and three centre integrals were evaluated exactly[9].

For clarity a second representation of the electrostatic energy is useful. The charge distribution is partitioned into segments each of which is assigned to an atomic centre[10]. An infinite series of interactions between the successive electric moments on the atomic centres of the hapten with those of the antibody site will converge to the value of equation (1). The charge of the nitrogen is just the monopole moment of that atom in this atomic multipole representation. The scheme of New and Richards ignores all other atomic monopoles (including those on the methyl carbons and hydrogens which closely approach the negative charge) as well as all higher moments.

Table 1 Comparison of Free Energies Calculated from Point Charge on N with that Calculated Rigorously

Hapten (Trimethylammonium ion)	Point charge	Equation (1)
p-Tolyl	9.9649	71.1171
m-Tolyl	9.8971	69.1563
o-Tolyl	9.1515	70.0352
Phenyl	9.9649	70.0508
p-Amino phenyl	9.5582	67.3571
p-Amino benzyl	9.7616	69.7268

All energies in kcal mol^{-1}.

The importance of the neglected terms is indicated by Table 1, which shows that the charge on the nitrogen accounts for only a small fraction of the binding energy and that the correlation between binding energy and charge density therefore becomes meaningless.

Table 2 Relative Binding Energies Calculated (Rigorously) and Obtained Experimentally*

Hapten	Calculation	A	Experiment B	C
p-Tolyl	− 1.066	−0.206	−0.105	−0.105
m-Tolyl	+ 0.895	+0.084	+0.291	—
o-Tolyl	+ 0.016	+0.041	+0.077	+0.123
Phenyl	—	—	—	—
p-Amino phenyl	+ 2.694	+0.041	+0.077	+0.090
p-Amino benzyl	+ 0.324	+0.256	+0.406	+0.430

* (Refs. 4 and 5) for three different antibodies in kcal mol^{-1}.

In Table 2, the more rigorously calculated relative binding energies are shown, in some cases, to have a better correlation with experiment than given by the point charge model, but they still fall short of an overall quantitative correlation. An explanation of this lack of correlation comes from a consideration of the magnitude of the forces involved. The intrinsic electrostatic attraction between a hapten and the antibody site at Van der Waals's distance is of the order of 70 kcal mol^{-1}, while the relative binding energy is approximately 0.2 kcal mol^{-1}. In the hypothetical case of two haptens with identical charge distributions interacting with identical antibodies, where the local dielectric constant is even as high as 5, factors altering the spatial relationships between reactive sites by as little as 0.1 Å would cause changes in the binding energies between

them in excess of 0.2 kcal mol^{-1}, greater than most differences in binding energies previously reported. This suggestion is consistent with the observations made by Burgen et al.[11] on the NMR spectra of similar hapten/antibody complexes.

We would suggest that the substituents exert three major effects on the binding. The first is the influence on the electronic structure of the group adjacent to and dominating the interaction with the site. The second is on the positioning of the hapten relative to the site. Third, surface area dependent solvent effects may significantly act on bulky substituents. As shown, the first may be computed to high accuracy. Theoretical techniques for solvent forces[12] exist and are currently being studied by us. Steric relationships can be determined, at least in principle, by physical techniques like NMR[13].

We conclude that in view of the subtle interplay of the above effects any attempt at rationalization of experiment binding data which arbitrarily disregards any of these factors can only be misleading.

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Radioimmunoassay of Luteinizing Hormone Releasing Hormone

THE isolation and characterization of hypothalamic luteinizing hormone releasing hormone (LH–RH) and its subsequent synthesis have made possible the production of an antibody specific for this decapeptide.

Unlikely to be immunogenic by itself, the LH–RH was haptenized to bovine serum albumin by the carbodiimide technique[1] and injected into New Zealand white rabbits. Antibody to LH–RH appeared within 2 months (unpublished results).

Synthetic LH–RH was iodinated by the method of Hunter and Greenwood[2], using 5 µg of LH–RH and 1 mCi of ^{125}I-iodide. The labelled hormone was separated from inorganic iodide by passage through a column of 'Sephadex G-10'. Specific activities of 47–85 µCi µg^{-1} were achieved.

The antibody to LH–RH was able to bind the labelled hormone and at a final antibody dilution of 1 in 1,200, 58% of the labelled hormone was bound.

Storage of the labelled hormone at $-20°$ C for 4 weeks did not reduce its ability to combine with the antibody.

The binding of the labelled hormone was not affected by various polypeptides, including thyrotrophin-releasing hormone, human thyroid-stimulating hormone (TSH), ovine prolactin, ovine luteinizing hormone, human chorionic gonadotrophin, adrenocorticotrophic hormone (ACTH) and the synthetic 1–24 amino-acid chain of ACTH. These available polypeptides were present in amounts ranging from 1 to 10^5 ng.

LH–RH and the octapeptide (TRP-SER-TYR-GLY-LEU-ARG-PRO-GLY-NH$_2$), lacking only the pyroglutamyl and histidyl residues from the N-terminal sequence of LH–RH, produced virtually identical decreases in the binding of the labelled hormone.

Table 1 Antibody Binding of ^{125}I–LH–RH in the Presence of Unlabelled LH–RH

ng unlabelled LH–RH	0	0.09	0.19	0.47	0.94	1.9	3.8	9.4
% ^{125}I–LH–RH bound	21.9	20.0	19.0	16.7	14.9	13.3	10.7	2.1

0.1 ml. of LH–RH solution, 0.1 ml. of antiserum (1 in 4,500), 0.1 ml. of rabbit serum (1 in 100), 0.1 ml. of 0.05 M phosphate buffer, pH 7.2 (0.02 M EDTA, 0.15 M NaCl).

Incubated at 4° C for 48 h. Added 0.1 ml. of ^{125}I–LH–RH, incubated 72 h at 4° C. Added 0.1 ml. of anti-rabbit γ-globulin (donkey), 1 in 20. Incubated over 24 h at 4° C. Centrifuged at 2,000g for 30 min. Radioactivity in precipitate counted.

The addition of increasing amounts of unlabelled LH–RH produced the decreases in the binding of iodinated hormone shown in Table 1. In these conditions assays carried out in triplicate gave coefficients of variation of 1–4% at low LH–RH concentrations. The lowest concentration of LH–RH used (0.09 ng) gave a reduction of 9% in the amount of antibody-bound radioactivity relative to that found when no unlabelled hormone was present. The detection level in this assay is therefore 0.09 ng or better.

The stability of the iodinated LH–RH in the presence of serum was studied. Incubation for 4 h at 37° C of LH–RH (20 ng ml.$^{-1}$) either in serum, or in 0.05 M phosphate buffer, pH 7.2, or in serum containing 1,500 KIU of Trasylol did not significantly reduce binding. Further incubation for 4 days at 4° C was also without effect.

Samples of plasma obtained from twelve young, healthy females over days 10–17 of the menstrual cycle have been assayed using the procedure outlined but no measurable amounts of LH–RH have been detected. This is possibly due to the relatively insensitive nature of the present assay system or to the time of collection of the plasma samples.

The concentrations of LH–RH in the general circulation will probably be extremely low. It would seem reasonable, however, to conclude that the basis of a specific and sensitive assay for LH–RH exists. Further work is being undertaken to try and increase substantially the sensitivity of the assay in order to detect the hormone in plasma, cerebrospinal fluid, or other biological fluid.

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Growth of Abnormal Cells

INVESTIGATIONS have been made using the model for the growth of abnormal cells suggested by Williams and Bjerknes[1]. They showed that the mathematics of the problem remained largely the same for different cell lattices, and so, for reasons of programming simplicity, consideration is limited to growths on square lattices.

Each growth begins with a single abnormal cell situated at the (approximate) centre of a lattice of normal cells. A probability $\kappa/(\kappa+1)$ (κ can be considered as the "carcinogenic advantage") is assigned to the event in which an abnormal cell divides and the subsequent abnormal daughter cell replaces one of the neighbouring normal cells. Similarly regression can occur, and there is a probability of $1/(\kappa+1)$ that one of the abnormal cells is pushed out of the layer by a normal daughter cell.

For infinitely large values of κ—that is, regression is impossible—the model is greatly simplified, and the mathematics becomes considerably more tractable. At each step of the "no-regression" model, it can be proved that when there are n abnormal cells, the number of links l_n between normal and abnormal neighbours lies in the range $(4\sqrt{n}, 2(n+1))$. It follows that if ET_n is the expected time for growth to n abnormal cells, then

$$\tfrac{1}{2}\ln((n+2)/2) < ET_{n+1} < m/2 - (\ln(m+\tfrac{1}{2}))/8 + A' \qquad (1)$$

where m is the largest integer less than or equal to $\sqrt{n}$ and where the constant $A' < 0.27$.

The following improved lower bound can be obtained using a conjecture of Morgan and Walsh[2] and a result of Hammersley[3]. For large n

$$ET_n \geq K'\sqrt{n} + K'' \qquad (2)$$

where $0 < K' < 1$ and $K'' < 0$.

Because inequality (2) depends upon a conjecture, it does not disprove the results of Williams and Bjerknes[1], but it does imply that one should attempt to fit a growth function of the form $ET_n = A\sqrt{n} + f(n)$, where $f(n)/\sqrt{n} \to 0$ as $n \to \infty$.

The computer used in this study was a KDF9 with 32k words of core store. This is an old machine and so it was absolutely necessary for the programming to be done efficiently. By careful addressing, we were able to obviate searching: that is, once a random number had been generated, the cells concerned were located immediately and the necessary adjustments to the listings made. For the model with no regression ($\kappa = \infty$) the computer time required for a "growth" of 10,000 abnormal cells was a little more than 1 min. This time rises quite dramatically for κ less than about 10. Thus for models in which there is regression, "growths" are limited to 1,600 abnormal cells.

The results of the simulations show that the estimated values of ET_n lie much nearer to the upper bound than the lower bound in inequality (1), and we decided to fit a function of the form

$$ET_n = A\sqrt{n} + B\ln(\sqrt{n} + \tfrac{1}{2}) + C \qquad (3)$$

The logarithmic term was included as it occurs in both bounds and could well be an inherent characteristic of the growth function. For large n, the first term in equation (3) becomes dominant, in agreement with inequality (2).

Williams and Bjerknes[1] fitted

$$ET_n = \beta n^{\alpha} \qquad (4)$$

to the results of their simulation. We fitted both equations (3) and (4) to our results using least squares and weights inversely proportional to the variances; the observed values and the fitted values are given in Tables 1 and 2.

Table 1 Mean Time to 10,000 Abnormal Cells for Forty Computed Growths

No. of abnormal cells	Observed values of ET_n	Fitted values of ET_n W-B model (4)	D-M model (3)
25	1.65532	1.67669	1.65422
100	3.19619	3.14713	3.20236
225	4.58628	4.54862	4.60202
400	5.93916	5.90713	5.93823
625	7.24513	7.23456	7.23902
900	8.52198	8.53772	8.51718
1,225	9.79807	9.82105	9.77961
1,600	11.03331	11.08764	11.03047
2,025	12.27138	12.33978	12.27246
2,500	13.51333	13.57921	13.50744
3,025	14.73671	14.80732	14.73673
3,600	15.95674	16.02524	15.96131
4,225	17.17168	17.23388	17.18193
4,900	18.39132	18.43404	18.39919
5,625	19.60564	19.62636	19.61352
6,400	20.82619	20.81142	20.82533
7,225	22.03870	21.98971	22.03489
8,100	23.24424	23.16167	23.24249
9,025	24.44721	24.32767	24.44831
10,000	25.65223	25.48807	25.65255

Parameter values for W-B model are $\alpha = 0.4542$, $\beta = 0.3886$, standard error $= 0.0686$.

Parameter values for D-M model are $A = 0.23496$, $B = 0.57741$, $C = -0.5049$, standard error $= 0.0074$.

The extrapolated values of ET_n for small n ($n = 1, 2, \ldots 9$) are given in Table 3. The exact values for ET_n ($n = 1, 2, \ldots 9$) were calculated by considering all possible configurations, and they are included to facilitate comparisons.

The Tables show that in all cases, equation (3) provides a better fit than equation (4). Even in growths up to 10,000

abnormal cells, however, equation (4) provides a good fit to the data. The value of the exponential coefficient α shows little difference from that obtained by Williams and Bjerknes[1] when fitting over the first 1,600 abnormal cells; α is still approximately 0.45.

This phenomenon can easily be explained. It can be seen in Table 1 that the mean time to 900 cells is approximately one-third of the time to 10,000 cells and, in general, the rate of growth increases as the number of abnormal cells increases. When considering the time to n abnormal cells for individual growths, we noticed that there was always a strong positive correlation between the time to 1,600 cells and the time to 10,000 cells; for example, if the time to 1,600 cells was less than the average time, then the time to 10,000 cells was also less than the average time. Consequently, the value of α in equation (4) does not change greatly when the results are fitted up to 10,000 cells.

Table 2 Mean Time to 1,600 Abnormal Cells for 250 Computed Growths

No. of abnormal cells	Observed values of ET_n	Fitted values of ET_n W-B model (4)	D-M model (3)
25	1.66050	1.67915	1.66038
100	3.18535	3.14749	3.18588
225	4.57621	4.54555	4.57776
400	5.91260	5.89983	5.91253
625	7.21631	7.22246	7.21543
900	8.50250	8.52041	8.49796
1,225	9.76662	9.79819	9.76634
1,600	11.02044	11.05894	11.02430

Parameter values for W-B model are $\alpha = 0.45323$, $\beta = 0.39039$, standard error $= 0.03088$.

Parameter values for D-M model are $A = 0.23790$, $B = 0.51964$, $C = -0.41495$, standard error $= 0.00255$.

To illustrate that $\alpha \rightarrow 0.5$, we fitted equation (4) to the variable ($T_n - T_{1,600}$) using least squares and weights inversely proportional to $\mathrm{var}(T_n - T_{1,600})$. Under these circumstances $0.48 < \alpha < 0.485$. When equation (4) is fitted to the variables ($T_n - T_{3,600}$) and ($T_n - T_{400}$), α is found to be approximately 0.49 and 0.472 respectively. It seems therefore that ET_n is indeed tending towards a function of the form $A\sqrt{n}$ as n becomes large.

Table 3 Extrapolated Values of ET_n for $n = 1, 2, \ldots 9$

No. of abnormal cells	Exact values of ET_n	Extrapolated values of ET_n W-B model (4)	D-M model (3)
1	0.00000	0.39039	0.03364
2	0.25000	0.53448	0.25889
3	0.41667	0.64231	0.41432
4	0.54167	0.73176	0.53698
5	0.6458	0.80964	0.64003
6	0.7358	0.87939	0.72983
7	0.8160	0.94303	0.80999
8	0.8885	1.00186	0.88278
9	0.9551	1.05680	0.94972

Finite values of κ were then considered and the function (3) was again used as a fit to the observed data. Table 4 shows the parameter values obtained for both models for certain values of κ, and the standard deviations are included to illustrate that, once more, our fit seems to be better than that of Williams and Bjerknes[1].

Table 4 Parameter Values and Standard Errors for Both Models over 100 Computed Growths up to 1,600 Abnormal Cells

| Value of κ | D-M model (4) | | | Standard error | W-B model (3) | | Standard error |
	A	Parameter values B	C	s	α	Parameter values β	s
∞ (250 growths)	0.23790 (0.23914)	0.51964 (0.50693)	−0.41495	0.00255	0.45323	0.39039 (0.3903)	0.03088
50	0.24052 (0.24136)	0.53494 (0.52248)	−0.43151	0.00547	0.45303	0.39621 (0.3956)	0.03325
20	0.24241 (0.24486)	0.56032 (0.54703)	−0.44599	0.00885	0.45091	0.40801 (0.4040)	0.03591
10 (98 growths)	0.25097 (0.25121)	0.59442 (0.59158)	−0.47121	0.00733	0.4497	0.42778 (0.4192)	0.03561
5 (96 growths)	0.26926 (0.2663)	0.65041 (0.69740)	−0.51644	0.00526	0.44924	0.46198 (0.4554)	0.04116
3 (82 growths)	0.29815 (0.29346)	0.87830 (0.88786)	−0.90934	0.00541	0.45967	0.48626 (0.5204)	0.11298
2 (81 growths)	0.34484 (0.34777)	1.28406 (1.26880)	−1.21705	0.02291	0.44351	0.66475 (0.6505)	0.13434

"Growths" which regress to zero after one step are not included. A, B and β were fitted to $\lambda + \mu/(\kappa-1)$ using least squares; the fitted values are given in parentheses.

If $E[T_n|\kappa]$ is the expected time to n abnormal cells for a given κ, and if we conjecture that $E[1/l_n|\kappa] \le E[1/l_n|\infty]$, then using the theory of recurrent events the ratio $E[T_n|\kappa]/E[T_n|\infty]$ can be shown to lie in the range $[1, 1+2/(\kappa-1)]$. Thus the replacement of β in equation (4) by (constant/$(\kappa-1)$) is invalid.

The parameters A, B and β in equations (3) and (4) are obviously functions of κ, the forms of which we have been unable to establish theoretically. A, B and β have, however, been fitted, using least squares, to $\lambda + \mu/\kappa-1$) and the fitted values are given in parentheses in Table 4.

In conclusion, it seems reasonable to suppose that the growth function tends to a function of the form $A\sqrt{n}$ if large enough values of n are considered. Our results are in agreement with Williams and Bjerknes and remain so for n as large as 10,000. If, however, the "transient" part of the growth function is extracted by considering variables such as $(T_n - T_{1,600})$ for each growth, we approach the "steady state" situation and α tends to 0.5.

<div style="text-align:right">

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Renal Blood Flow in a Diving Trained Sea Lion

THE diving reflex described for many species of animals involves a reduction in heart rate and the redistribution of blood flow to various tissues. Available evidence[1,2] indicates that cardiac output decreases and that arterial pressure increases only modestly or remains unchanged during a dive. Flow measurements using restrained animals have tended to show cessation of flow to the kidney[3,4] with diving. But it is well accepted that differences in these responses will exist with restrained and frightened animals as opposed to trained or free ranging animals. We investigated peripheral blood flow in a trained sea lion (*Zalophus californiaus*) by measuring the renal flow

response to face immersion in water. Several months before surgery, the female sea lion was trained to place her head into a bucket, either empty or filled with water, and to remain in that position until otherwise commanded. During training, the animal wore a harness to which the necessary electronics were later attached.
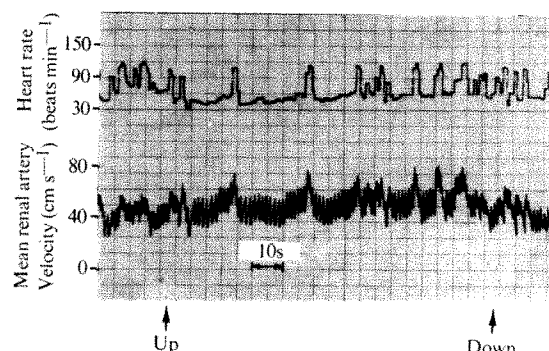
Fig. 1 Heart rate and mean renal artery flow velocity during breath holding or resting condition.

The animal was anaesthetized using a mixture of oxygen and fluothane after intramuscular injection of 0.020 mg kg^{-1} atropine. An 8 mHz Doppler flow cuff was implanted on the left renal artery under sterile surgical conditions. Care was exercised in the dissection of the artery so that minimal damage would be done to the perivascular renal nerves. The lead wires were tunnelled under the skin to the dorsal surface of the neck at which point they were brought through the skin. The mid-line incision was closed with interrupted sutures. For the next seven days, the animal was given oral antibiotics. Training was resumed about four days after surgery, but experiments were not performed until four weeks after the operation. The Doppler flow meter used followed the design of Franklin[5]. Recordings were made of mean renal artery flow velocity and heart rate using the flow velocity pulse to trigger the cardiotachometer. Jugular vein blood samples were obtained both pre- and post-operatively for red and white cell counts.

We show a representative portion of a control recording in Fig. 1. The resting heart rate on this occasion was 75 beats min^{-1} and the control velocity was 45 cm s^{-1}. The "down" arrow indicates the immersion of the animal's head into an empty bucket and the "up" arrow indicates the reverse. Breath holding periods can be observed with the heart rate as

low as 36 beats min^{-1} and the mean renal artery velocity varying with the rate. Thus breath holding in this situation was part of the effect of training. The average resting heart rate was 85 beats min^{-1} and the average resting mean renal artery velocity was 48 cm s^{-1} for this animal during all of the experimental periods.
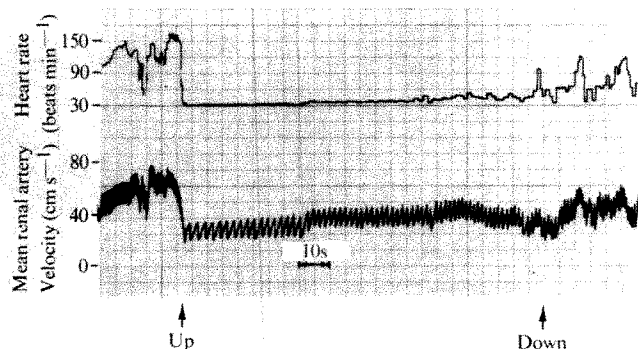
Fig. 2 Heart rate and mean renal flow velocity during face immersion for 2 min.

The record shown in Fig. 2 was obtained during an immersion in water lasting 2 min. A respiratory sinus arrhythmia occurred prior to immersion (right hand edge Fig. 2). Upon immersion a striking bradycardia began, with nadir of 30 beats min^{-1}. A reduction in mean renal artery velocity to 28 cm s^{-1} also occurred with some over-shoot in flow at the termination of the dive. The average length of 16 dives by the animal was 80 s. The mean heart rate at the end of the dive was 34 beats min^{-1} and the mean renal artery velocity was 31 cm s^{-1}, which represents an average reduction of 34% below the control value. The health status of the animal as evaluated by red and white cell counts from jugular venous blood were almost identical. Because velocity is related to volume flow by the cross-sectional area of the vessel, which is fixed in the present experiment, inferences about flow can be made.

From the studies in this unrestrained animal, it seems that inflow to the kidney does not cease but is reduced together with the cardiac output as has been shown in the duck[6]. We offer three possible explanations for the variance from previous studies: First, intrarenal redistribution of blood flow; second, species difference; third, fright. Intrarenal redistribution of flow has been demonstrated in the kidney of non-diving mammals[7,8]. There is no way to rule out species difference; but fright is known to produce severe reaction in all animals. The record (Fig. 2) also demonstrates that there is an immediate reduction in flow, as occurs with cardiac output; thus these reductions are of neural origin. The delayed reduction in renal flow and the post-dive over-shoot of the flow response are probably related to the duration of the dive. Afferent signals of renal origin may influence the duration of diving. Therefore, oxygen may be conserved in the kidney by shunting blood around highly metabolic areas such as cortex, and simultaneously these shunts may be used to adjust vascular resistance to ensure adequate perfusion of the heart and brain and to reduce the work of the heart specifically.

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Protection against Enteric Disease caused by *Escherichia coli* – a Model for Vaccination with a Virulence Determinant?

ALTHOUGH vaccination has assisted the control of many bacterial diseases, parenteral vaccination against enteric disease is not as satisfactory as we could wish[1]. This is attributable to incomplete knowledge of both the pathogenesis of intestinal infections and the protective immune responses of the alimentary tract, with the result that vaccine development has been largely empirical. New knowledge of the specific determinants of microbial pathogenicity[2] provides a sounder basis for the development of effective vaccines and the following report is an example of this approach to disease control.

The pathogenesis of porcine neonatal diarrhoea involves colonization of the intestine by an enteropathogenic strain of *Escherichia coli*[3] followed by production of enterotoxins[4-7]. Most strains of *E. coli* that cause neonatal diarrhoea synthesize one of two closely related protein surface antigens designated K88ab or K88ac[8-10]. The K88 antigen has adhesive properties that seem to be essential for the virulence of K88-positive enteropathogenic strains of *E. coli*[11] and enable K88-positive bacteria to proliferate in the anterior small intestine[12]. Thus, the two important virulence determinants of these strains of *E. coli* are (i) K88 antigen, which enables the bacteria to attach and attain large numbers in the small intestine, and (ii) enterotoxins, which cause severe diarrhoea, resulting in dehydration and death.

From these observations, we deduced that piglets could perhaps be protected against neonatal diarrhoea either by preventing bacterial attachment to the intestinal wall or by neutralizing the effects of enterotoxins. Antibodies directed against enterotoxins may be protective[13,14], but protection has also been observed which seemed to be antibacterial rather than anti-enterotoxic[15,16]. Attachment of K88-positive bacteria to piglet intestinal tissue can be demonstrated *in vitro* and is inhibited by K88 antisera[11]. Therefore, the antibacterial activity described *in vivo* could be due to an anti-K88 factor which prevents bacterial adhesion. There is no detectable placental transfer of antibodies in the pig[17,18]; so we postulated that K88 antibodies transmitted via the colostrum to the piglet's intestinal tract should reduce attachment of K88-positive enteropathogenic bacteria to the mucosa and render the organism less virulent.

We investigated this hypothesis by immunizing pregnant gilts with partially-purified K88 antigens, then challenging their piglets with a virulent K88-positive strain of *E. coli*. K88 antigens were extracted from two laboratory-derived K88$^+$ strains [08:K27(A)$^-$, K88ab:H$^-$ and 08:K27(A)$^-$, K88ac: H$^-$] prepared by introducing the plasmids which determine

synthesis of either K88ab or K88ac antigens[12,19] into a K⁻H⁻ mutant [08:K27(A)⁻:H⁻ kindly provided by Dr Ida Orskov, Statens Seruminstitut, Copenhagen] of a human peritonitis strain. No enterotoxins were detected in these two K88⁺ strains. K88 antigens were precipitated from cell-free homogenates by acetic acid[9,11]; precipitates contained 98% (w/w) protein, (predominantly K88 antigen), 0.5% (w/w) carbohydrate and 1.5% (w/w) nucleic acids. Equal amounts of K88ab and K88ac antigens were incorporated in a water-in-oil emulsion[20], and emulsion containing 15 mg of K88 antigens was inoculated into a posterior mammary gland of four gilts 11 weeks before parturition. A saline suspension containing 30 mg of K88 antigens was given subcutaneously in the flank 10 days before parturition. Four control gilts received a primary inoculation of saline emulsion and a second injection of saline.

Approximately 1×10^{10} viable organisms of the 0149:K91 (B), K88ac(L):H10 serotype of E. coli were given orally to the piglets at birth before sucking[15]. All piglets showed clinical signs of neonatal diarrhoea within 24 h of challenge. In the four litters from non-vaccinated gilts, twenty of twenty-nine piglets died of experimental neonatal diarrhoea (END) within 72 h; the viable counts of the enteropathogenic strain in the anterior small intestine were $10^8 - 10^9$ per gramme of contents. In contrast, only four of thirty-one piglets from vaccinated gilts died of END) and the clinical signs were less severe. The reduction in mortality between piglets from vaccinated and non-vaccinated gilts is statistically significant ($P < 0.01$ in a one-tailed t test).

It seems that K88 antibodies in colostrum were responsible for protection because (i) the vaccine was prepared from laboratory-derived strains of E. coli which apparently resemble the challenge strain only with respect to K88 antigens and (ii) antibodies against K88 were detected in immunodiffusion tests with colostrum from vaccinated gilts. These conclusions are supported by a report that the protective effect of antisera administered orally to piglets seemed to be directed against K88 antigens[21]. Thus, vaccination of the dam with K88 antigens provides passive protection for her piglets against challenge with a K88-positive strain of E. coli; protection should also be afforded against other enteropathogenic K88-positive E. coli. The reduced mortality among piglets from vaccinated dams suggests that the challenge strain was unable to attach and attain large numbers in the small intestine, and studies are in progress to confirm that K88 antibodies in colostrum are anti-adhesive.

Parenteral vaccination against enteric infections caused by Gram-negative bacteria is regarded as unsatisfactory because the vaccines are frequently ineffective, protection is transient or because of side-reactions associated with endotoxins. Oral prophylaxis with attenuated bacteria has potential advantages but inherent dangers are associated with the administration of live organisms. An alternative approach is to recognize the virulence determinants of enteropathogenic bacteria and to stimulate the production of protective immune responses to these determinants. Bacterial adhesive factors must be surface components and may be detectable as surface antigens. If attachment of an enteropathogenic group of bacteria to the intestinal wall is an important determinant of virulence, strains within that group should produce similar adhesive factors and hence have similar surface antigens. Strains of Vibrio cholerae[22] and strains of E. coli that are enteropathogenic for infants[23,24] or calves[25] attach to intestinal mucosa and common antigens have been detected in each of these groups[26-28]. These antigens deserve further investigation to determine if they are necessary for virulence.

Although our results refer to only passive protection, vaccination with K88 antigens could provide both a practical method for controlling porcine neonatal diarrhoea and a model for investigating a protective mechanism in the alimentary tract. This approach to microbial pathogenicity may lead to the incorporation of concentrated, purified virulence determinants in parenterally or orally administered vaccines.

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Anti-bacterial Substances in Hypersensitive Responses induced by Bacteria

WHEN an avirulent fungus infects resistant plant tissue it often kills only a small number of cells and remains confined to the dead cells. This acute, very localized reaction is referred to as a hypersensitive response. When the pathogen is not an obligate biotroph, death of these cells need not explain why it does not continue to grow. In certain diseases caused by such pathogens growth is prevented because substances toxic to the pathogen accumulate at the locus of infection. Such substances are now commonly referred to as phytoalexins; in diseases of

parenchyma there is some evidence that they are largely confined to the killed cells or those immediately adjacent[1].

Plant tissues may react in a similar manner to bacterial pathogens though the process is somewhat different because individual cells are not penetrated. But with suitable techniques it can be shown that numbers of viable bacteria increase little if at all after hypersensitive response has developed; although their numbers are low, avirulent bacteria are readily recovered from tissues showing this response. Here, too, death of host cells as such does not explain the effects on multiplication of the avirulent bacteria. The phytoalexin phaseollin does accumulate in hypersensitive responses in leaves of French bean (*Phaseolus vulgaris*) caused by avirulent bacteria but this substance has little or no effect on growth of bacteria[2]. Unknown substances accumulate in resistant bean tissues which inhibit the growth of the saprophyte *Brevibacterium linens*[3]. We now report on the accumulation in bean leaves of anti-bacterial substances, which probably explains why avirulent bacteria do not continue to multiply in resistant plant tissues.

French bean plants, cultivar Red Mexican, are susceptible to race 2 of the halo blight bacterium *Pseudomonas phaseolicola* but give a typical hypersensitive response to race 1, as they do to *P. mors-prunorum*, a pathogen of stone fruit trees. The saprophyte, *P. fluorescens*, causes no visible response in bean leaves.

Leaves were inoculated by injecting air spaces with suspensions of each of the bacteria; 1, 2 and 5 days later leaves were extracted with 95% EtOH. The residue after evaporation of the EtOH was taken up in water, acidified to pH 4.0 and shaken with equal volumes of ethyl acetate. Substances soluble in ethyl acetate or water were applied to 0.25 mm G nach Stahl silica gel TLC plates which were developed in methanol : chloroform (4 : 96 v/v), dried and then sprayed with suspensions of *P. phaseolicola* races 1 and 2, and *P. mors-prunorum* in a buffered nutrient medium (pH 7.5). The plates were incubated for 48 h in about 100% RH at about 25° C and then sprayed with a solution of tetrazolium salt (1% w/v). Areas in which bacteria failed to grow appeared white, against a pink background where bacteria had grown and in which the tetrazolium salt had been reduced by their dehydrogenases.

Three prominent areas in which bacterial growth had been inhibited had R_F values of 0.32, 0.29, 0.17 on developed plates of ethyl acetate solubles of 1, 2 and 5 day extracts of hypersensitive tissue. These areas did not appear on plates with extracts from leaves 1 or 2 days after inoculation with virulent race 2 of *P. phaseolicola* or with *P. fluorescens*. But they were found in extracts from susceptible leaves with typical water soaked lesions 5 days after inoculation with race 2.

Also five much less prominent areas of inhibition appeared in chromatograms of all extracts and two or three were sometimes found only in extracts of hypersensitive tissues. No inhibitory areas were seen on developed plates of water soluble substances.

The first three compounds were eluted from TLC plates with ethanol and purified in TLC chromatograms with benzene : acetone (50 : 50 v/v), methanol : chloroform (10 : 90 v/v), and toluene : chloroform : acetone (40 : 25 : 35 v/v). They were tested for anti-bacterial activity *in vitro* by placing impregnated filter paper disks on agar seeded with sensitive bacteria. There was no inhibition of growth when disks contained 0.5 to 5 times the amount of subtances contained per gram fresh weight hypersensitive tissue 1 day after inoculation.

But when incorporated into a liquid medium (nutrients as in the agar) with a solubilizing agent (propylene glycol), and at a concentration 0.5 times that in leaves 1 day after inoculation, two of the compounds prevented growth of *P. phaseolicola* races 1 and 2, and *P. mors-prunorum* for 36 h, and the third compound did so for the whole of the 72 h incubation period. Further tests showed that the compound was bactericidal at this concentration.

The partially purified compounds had characteristic ultra-violet spectra, gave a positive reaction with diazotized sulphanilic acid reagent, fluoresced strongly at 254 and 366 nm and showed spectral shift on addition of NaOH (2N) to ethanolic solutions. This and other evidence suggests that the compounds are phenolic; we will study their structure further.

These compounds can be obtained from hypersensitive tissue when numbers of viable bacteria stop increasing. Examination of this tissue which macroscopically appears necrotic shows that 20–33% of the cells are brown and presumably dead. These are the cells that fluoresced brightly under UV microscopy and may, therefore, be the only ones that contained the antibacterial substances. This is also suggested by the fact that these substances cannot be extracted from green tissue immediately outside brown, hypersensitive tissue. It is probable, therefore, that local concentrations of these inhibitors around bacteria that induce hypersensitive responses in cells are well in excess of those that prevent bacterial growth.

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Significance of Head Tilting in the Great Blue Heron

ONE of the problems confronting a bird that hunts for food over water is glare produced by the Sun. Several ways of reducing the interference of glare have been discussed, including both anatomical features such as dark patches around the eyes[1], coloured oil droplets in the retina[2] and polaroid filters[3], and behavioural mechanisms such as looking through the shadow of an outstretched wing[4]. We have observed what seems to be another behavioural device for reducing the hindrance of glare.

During the course of a study of the feeding behaviour of great blue herons (*Ardea herodias*) we noticed that often when a heron that was hunting was seen head on, its head and neck were tilted quite markedly to one side (Fig. 1). This posture was often maintained for several minutes while the heron walked slowly through the water, occasionally orienting (suddenly turning the head) to or striking at prey. Thus head tilting was not simply a form of orienting to, or looking at, a potential prey item, nor was it a form of head swaying movement which might be used to obtain a parallax estimate of distance to the prey[2]. Although the two can occur simultaneously, head tilting is distinct from head cocking, in which the bird holds its head on one side, perhaps for the purpose of monocular scanning[5,6].

Meyerreicks[4,7] has apparently observed a similar phenomenon in the reddish egret (*Dichromanassa rufescens*) and little blue heron (*Florida caerulea*) and he coined the term head tilting.

We subsequently noted that head tilting was much commoner on sunny days (also noted by Meyerreicks[4]) and only occurred when the heron was facing at an angle to the Sun (that is not directly towards or away from the Sun). Further, herons almost invariably tilted their heads towards the Sun (more than eight times as often towards as away). These observations

clearly indicated that head tilting is somehow related to the Sun and presumably to the effect of the Sun on the heron's ability to catch fish (the chief prey in our study were sculpins (*Leptocottus armatus*) and flatfish (*Platychthes stellatus*)).
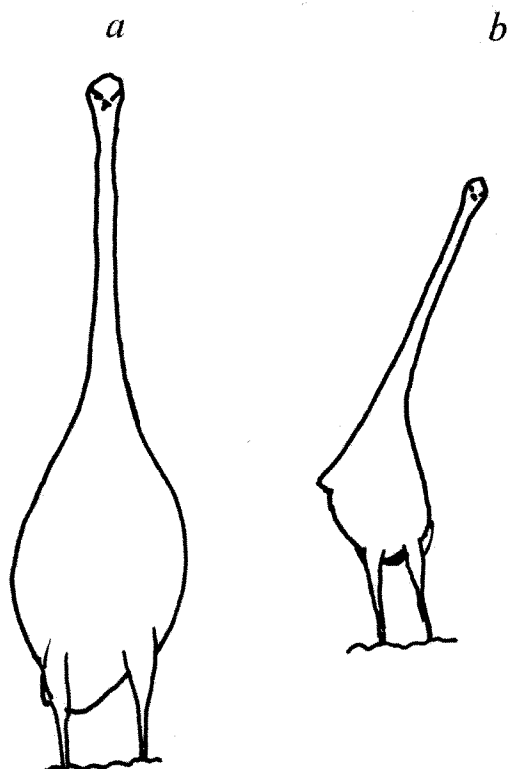
Fig. 1 Head-on views of two hunting herons traced from photographs taken (*a*) on a cloudy day and (*b*) on a sunny day. In (*b*) the bird is tilting its head towards the Sun.

Two types of hypothesis to explain how head tilting helps a heron hunt seemed plausible to us. (1) The prey have some reaction for avoiding predators which involves moving in a predictable direction with respect to the Sun. Thus if fish always tried to escape from herons by swimming towards the Sun (because, for example, they tried to get away from the bird's shadow), the heron might profit by leaning out towards the Sun and catching fish as they tried to escape. (2) Head tilting acts as a simple device to improve the bird's ability to see through the water and detect fish. Other hypotheses, for example, that head tilting is associated with enhancing detection of movement or perception of depth, seemed less likely to us, for they did not specifically require the bird to tilt towards the Sun. Head tilting could serve to reduce the hindrance of glare from the Sun in the following manner. If one stands in the water facing at an angle to the Sun, the Sun creates a patch of glare on the water surface just to the side of one's body that faces towards the Sun (the exact position and shape of the glare patch depend on body orientation and the height of the Sun, and the glare seems to be more distracting in turbid water). By leaning towards the Sun, one can slightly shift the glare patch further away from the area immediately in front of the body (Fig. 2). If we assume that the heron is confronted by similar problems, head tilting could serve as a device to shift the glare patch to one side and out of the normal range of reach (and therefore out of the region of water in which the bird is looking for fish). The heron would hunt in the glare-free area in front of and a little to each side of its body (Fig. 2).

If the first hypothesis is correct, the heron should strike at fish most often in the area immediately below its tilted head (to the right of the body in Fig. 2). The second hypothesis,

on the other hand, makes no particular prediction as to which direction the heron should strike in most often and one might expect the bird to strike with roughly equal frequency towards and away from the head-tilting direction as the available searching area is equal on both sides. Table 1 shows that, for a small sample of observations, herons struck at and/or caught fish with equal frequency on either side. The birds did, however, orient more often to the tilt side. Thus the data show that the herons have at best only a weak preference for hunting on the side to which they are tilting. This evidence favours the second hypothesis.

Table 1 Frequency with which Herons Struck and/or Caught Fish, or Oriented* toward Fish, towards and away from the Direction of Head Tilting

	Towards	Away
	from direction of head tilt	
Strike/catch	21	14†
Orient	34	18‡

* Orientation is a sudden movement of the head or neck, which presumably indicates that the bird is attending to something in the water.

† $\chi^2 = 1.4$, not significant.

‡ $\chi^2 = 4.92$, $P < 0.05$.

We examined the "glare" hypothesis further by training a hand-raised heron to hunt for dead fish in an indoor pool (4 m × 5 m, water depth 15 to 20 cm). We tested to see if it was possible to induce head tilting by means of an artificial sun (a 500 W photoflood lamp mounted on a stand at one edge of the pool 1 to 2 m above the water surface and pointing downwards). The room was completely blacked out so that the only source of glare was the "sun". These tests showed that the artificial glare did produce head tilting even in a naïve bird which had only hunted for dead fish. The bird could be induced to tilt its head to the right or left by moving the artificial sun from one side of the pool to the other; the bird always tilted towards the "sun". Head tilting was more marked if the water was made turbid. This result also supports the glare hypothesis, although it does not eliminate the
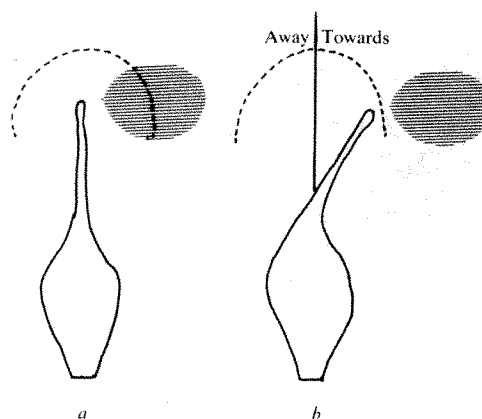
Fig. 2 A diagram of a heron as seen from above, to show how head tilting could serve to shift the position of the glare patch relative to the region of water in which the heron is looking for food. As the bird tilts its head to the right (*b*) (direction of Sun) the glare patch (shaded area) stays constant relative to the bird's head and shifts out of the area within the bird's reach (dotted semicircle). The bird is now holding its head more or less at the right hand limit of its reach, and can catch fish either immediately below its head or to the left. The solid line shows how we divided the bird's field of reach into "towards" and "away from" the direction of head tilting when collecting the data in Table 1.

possibility that the naïve heron had some inborn knowledge of the (hypothetical) escape response of live fish and was tilting its head for this reason.

In summary, we suggest that head tilting by great blue herons (and other related birds) serves to move the glare patch from the Sun to one side of the body, and from the area in which the bird is looking for fish. This presumably enhances the hunting efficiency of the birds in sunny weather.

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Deep-water Mosses in Antarctic Lakes

MOSSES are generally considered to be land plants although a few species are found growing submerged in streams and shallow areas of lakes. But there is now increasing evidence that certain species are able to grow successfully in deep water, often forming the dominant vegetation[1,2]. We have made the first underwater observations on deep-water mosses growing in Antarctic lakes. A SCUBA diving survey was carried out on Signy Island, South Orkney Islands (60° 43′ S, 45° 38′ W) in 1971 and 1972.

Signy Island lies within the Maritime Antarctic zone[3]. The influence of the surrounding ocean is shown by the relatively small temperature range (monthly mean $+0.8°$ to $-10.5°$ C; annual mean $-4.0°$ C), the high annual mean cloudiness (7 okta) and the low annual mean sunshine (1.5 h day^{-1}). The amount of snowfall is low (40 cm water equivalent yr^{-1}), although the frequency is high (335 day yr^{-1}). The area is extremely windy (annual mean 7.6 m s^{-1}, ref. 4).

The lakes are small and typically consist of a steep sided trough, 3–15 m deep, surrounded by a shelf formed by moraine damming. The shelf rarely exceeds 1 m in depth and is covered by scree and ground moraine, while the floor of the trough is of silt and mud broken by occasional projecting rocks[4]. The waters are soft, $pH \sim 7$, and are contaminated to a varying degree by sea spray and effluent from seal wallows and bird colonies[5]. Nitrate and phosphate levels are generally high (recorded summer range NO_3-N 190 to 19,000 µg l.$^{-1}$; PO_4-P 1 to 100 µg l.$^{-1}$). The lakes freeze to depths of 1–2 m for 8 to 12 months of each year, during which period an inverse thermal gradient develops, temperatures rising to around 1° C in the bottom layers. The waters of most lakes are very transparent but snow cover usually reduces the irradiance to a level below that thought to be necessary for photosynthesis for six months of the year, less than 1% of total visible incident light reaching the ice–water interface. In summer the waters attain temperatures of around 5° C and are isothermal, being stirred by strong winds.

Table 1 Distribution of Deep-water Mosses on Signy Island

Moss species	1	2	Lake number 4	6	9	14
Amblystegium sp.	×	×	—	×	—	×
Calliergon sarmentosum	—	—	×	—	×	×
Drepanocladus cf. aduncus	—	× *	×	—	—	—
Drepanocladus sp.	×	—	—	—	—	—
Pohlia nutans	—	—	—	—	—	×

The lakes have been described by Heywood[4,5].

No mosses were seen in Lakes 3, 5, 10, 11, 12 and 15.

* Specimen obtained by dredge in 1966 (R. I. Lewis-Smith, personal communication). Not observed by us in 1971.

There are no emergent macrophytes and, prior to our survey the vegetation was thought to consist of algae only. We found mosses growing in 6 of the 12 lakes surveyed (Table 1) and recognized two distinct communities. One, consisting of Amblystegium sp. or Pohlia nutans, was limited to the relatively few areas of rock, stones and gravel existing at depths below 2 m. The cover was discontinuous and the colonies were attached firmly to the substrate. The second community, consisting of Drepanocladus cf. aduncus, Drepanocladus sp. and Calliergon sarmentosum, occurred on mud and silt. The almost continuous cover often extended over areas of several square metres. In Lake 4, 40% of the bottom below 5 m was covered by a very luxuriant growth. Calliergon sarmentosum and Drepanocladus cf. aduncus occurred throughout the range of moss vegetation but the former was predominant in the shallower water and the latter at the greater depths. We observed in this lake an increase in stem length with depth, ranging from 10–20 cm at 5 m to 30–40 cm at 10 m. A similar phenomenon was observed by Bodin and Nauwerck in Lake Latnajaure, Sweden[1]. In 1972 one of us (J. J. L.) found Drepanocladus cf. aduncus, Calliergon sarmentosum and Campylium sp. growing on mud below 10 m in lakes on South Georgia in the sub-Antarctic. In one lake Drepanocladus cf. aduncus was growing luxuriantly at 30 m. Lakes on this island are not subjected to such prolonged periods of thick ice cover and overlying snow as lakes on Signy.

Drepanocladus cf. aduncus appears to be exclusively aquatic on Signy Island but the other mosses are terrestrial species which have become adapted to the aquatic environment. Calliergon sarmentosum, Drepanocladus sp. and possibly Amblystegium sp. are typically hydrophytic mosses. Pohlia nutans is a mesophyte, becoming almost xerophytic in some habitats. This species has developed a most atypical growth form in these lakes (S. W. Greene, personal communication). The mosses seem unable to withstand ice scour and no specimens were found where this could occur. Other factors apparently controlling inter- and intra-lake distribution were silting, substrate instability and annual light regime.

Deep-water mosses are known to occur elsewhere in Antarctica. In 1957 Russian scientists dredged luxuriant growths of moss from 33–36 m depth in ice-covered lakes in the Bunger Hills area (65° 54′–66° 24′ S, 100° 24′–101° 30′ E) of East Antarctica[6]. They made a similar discovery in the Schirmachervatna area (70° 45′ S, 11° 20′–11° 55′ E) in 1962. Although these lakes remain frozen throughout each year, prevailing winds keep the clear ice free of snow. Consequently a considerable amount of incident solar radiation enters the lakes during the greater part of the year[7,8]. The "polar night" at 70° S is less than 2 months long. Two of the mosses have

been described: *Bryum korotkevicziae*[9,10] and *Plagiothecium simonovii*[7].

Antarctic lakes seem to offer a more favourable physical environment for certain species than the surrounding land. In them, mosses are not subjected to desiccation, wide and rapid diurnal fluctuations in temperature, extremely low temperatures, freeze–thaw cycles and abrasion by wind driven ice crystals and granular snow—limiting factors for land vegetation[11]. The contrast is particularly marked in the "ablation window" areas of continental Antarctica (for example, Bunger Hills and Schirmachervatna) where the land vegetation is extremely sparse and often consists only of crustose lichens and moss cushions. Further, where established, the aquatic mosses seem to receive sufficient light annually for vigorous growth.

Studies on the ecology and production of the Signy Island aquatic moss communities will be carried out by the British Antarctic Survey.

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Increased Activity of the Peripheral Sympathetic Nervous System: Induction of Choline Acetyltransferase in the Preganglionic Cholinergic Neurone

PROLONGED increase in the activity of the peripheral sympathetic nervous system leads to augmented synthesis of tyrosine hydroxylase (E.C. 1.14.3.a) and dopamine β-hydroxylase (E.C. 1.14.2.1) in the terminal adrenergic neurone[1-6]. As the induction of these key enzymes in the synthesis of the adrenergic transmitter norepinephrine is mediated by increased activity of the preganglionic cholinergic nerves[2], the question arises, is the augmented utilization of acetylcholine also accompanied by increased synthesis of choline acetyltransferase (E.C. 2.3.1.6), the enzyme which is responsible for the formation of acetylcholine ?

We report here that treatment of rats with reserpine, which leads to a reflex increase in the activity of the preganglionic cholinergic nerves[7], produces augmented synthesis of choline acetyltransferase in the preganglionic cholinergic neurone, as determined in the superior cervical ganglion, where the total activity of this enzyme is confined to the preganglionic nerve terminals[8].

Male Sprague-Dawley rats weighing 100–110 g were injected subcutaneously with 7.5 mg kg^{-1} of reserpine and killed by a blow on the head 24 h later. Ganglia were removed and homogenized (in pairs) in 0.5 ml. of ice-cold 0.005 M Tris buffer (*p*H 7.4) containing 0.1% Triton X-100. The homogenates were centrifuged at 27,000*g* for 20 min at 0–5° C. Choline acetyltransferase activity was determined in the supernatant by the method of Fonnum[9], with modifications described in detail elsewhere[10]. Proteins were assayed according to the method of Lowry *et al.*[11].

Reserpine treatment resulted within 24 h in a marked increase of the *in vitro* activity of choline acetyltransferase, which amounted to 152% of controls in the superior cervical and to 161% in the stellate ganglion. Increased levels still persisted after 48 h (Table 1). If enzyme preparations of controls and reserpine treated animals were combined in various proportions the activity was always additive, that is, corresponding to the sum of the two components. This finding suggests that the increased activity does not result from the disappearance of an inhibitor or the formation of an activator, but rather from an increase in enzyme protein.

Table 1 Increase of Choline Acetyltransferase Activity in Ganglia after Treatment of Rats with Reserpine

| | Superior cervical ganglion | | Stellate ganglion | |
	nmol acetyl-choline h^{-1} per pair	nmol acetyl-choline h^{-1} mg^{-1} protein	nmol acetyl-choline h^{-1} per pair	nmol acetyl-choline h^{-1} mg^{-1} protein
Controls	3.60±0.28	16.7±1.0	2.78±0.24	13.9±1.6
Reserpine 24 h	5.12±0.62*	25.4±1.4*	4.30±0.34*	22.3±1.9*
Reserpine 48 h	4.92±0.58*	26.8±3.5*	4.71±0.61*	25.2±2.2*

Animals were injected subcutaneously with 7.5 mg/kg reserpine and killed after the time interval indicated. The concentration of choline in each assay was 10 mM, that of acetyl-CoA 0.1 mM. Each value represents the mean±s.e. of eight duplicate determinations.
* $P<0.001$, compared with controls.

To substantiate this assumption the effect of cycloheximide, an inhibitor of ribosomal protein synthesis[3,12,13], was studied. In these experiments determination of choline acetyltransferase activity was confined to the superior cervical ganglion (Table 2). The animals were treated with 0.9 mg kg^{-1} of cycloheximide every 6 h. The first dose was given at the same time as reserpine. The choline acetyltransferase activity was significantly ($P<0.025$) lower than that in animals treated with reserpine alone but did not differ significantly ($0.4>P>0.3$) from that of animals treated with cycloheximide alone. The small but statistically significant ($P<0.05$) increase in choline acetyltransferase activity after treatment with cycloheximide alone is probably due to a stress exerted by the drug and to the fact that the relatively low dose, which could not be increased without killing the animals before 24 h, does not completely inhibit protein synthesis[3]. The fact that the protein level is not significantly higher after reserpine treatment ($0.4>P>0.3$) shows that the increase in choline acetyltransferase activity is not a manifestation of generally increased protein synthesis but represents a specific effect as previously shown for the induction of tyrosine hydroxylase[1] and dopamine β-hydroxylase[6] in the terminal adrenergic neurone. In preliminary experiments an increase of choline acetyltransferase activity in superior cervical and stellate ganglia, very similar to the increase after reserpine treatment, was observed after exposure of rats to a relatively short (2 h) but intense stress by swimming to exhaustion.

Goldberg and Welch[14] have reported a marked increase in choline acetyltransferase activity of mice adrenals on intermittent psychosocial stimulation for 10 days[14]. Although the mechanism underlying the increased enzyme activity was not investigated, it seems reasonable to assume that an increased synthesis of new enzyme protein also takes place in these

Table 2 Inhibition of Reserpine-induced Increase of Choline Acetyl-transferase Activity in Superior Cervical Ganglia by Cycloheximide

	Choline acetyltransferase		
	nmol acetyl-choline h⁻¹ per pair of ganglia	nmol acetyl-choline h⁻¹ mg⁻¹ protein	Protein per pair of ganglia (µg)
Controls	3.46±0.29	14.4±1.1	241± 7
Reserpine	5.39±0.32*	22.7±0.7*	253±10
Cycloheximide	4.13±0.24†	18.4±0.8†	224± 6
Reserpine+ cycloheximide	4.28±0.30‡	19.4±1.2‡	227±13

Animals were injected subcutaneously with 7.5 mg kg⁻¹ reserpine 24 h before they were killed. Cycloheximide (0.9 mg kg⁻¹) was injected every 6 h for the same length of time. The concentration of choline in each assay was 10 mM, that of acetyl-CoA 0.1 mM. Each value represents the mean±s.e. of ten duplicate determinations except for the combined reserpine and cycloheximide treatment ($n=5$).
 * $P<0.001$, compared with controls.
 † $P<0.05$, compared with controls.
 ‡ $P<0.025$, compared with reserpine alone.

experimental conditions. Thus it appears that neuronally mediated induction of enzymes is not confined to the biosynthetic pathway of norepinephrine, but that a similar adaptation to increased transmitter utilization takes place in the preganglionic cholinergic neurone.

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Late Precambrian Microfossils: a New Stromatolitic Biota from Boorthanna, South Australia

OF the four dozen fossiliferous Precambrian sediments now known[1], only a very few contain diverse microfossil assemblages preserved in situ on which inferences of ecologic setting and evolutionary status can be based reliably. The time gaps between these deposits are enormous, commonly approaching or exceeding a duration equivalent to that of the entire

Palaeozoic. Present inferences regarding the course of early evolutionary development are therefore highly speculative. There is obvious need for the detection of additional evidence with which to evaluate such inferences and to fill in the skeletal picture that has emerged in recent years. We report here the discovery of a well preserved, stromatolitic microbiota from the late Precambrian of Boorthanna, South Australia, that should contribute measurably toward this goal.

In organization, mode of preservation, and ecologic setting, the newly discovered microbiota seems comparable to the benchmark Precambrian assemblages of the Gunflint[2], Beck Spring[3] and Bitter Springs cherts[4]. Like these assemblages, this microflora comprised a mat-building photosynthetic community that was permineralized by silica near the sediment–water interface in a shallow, presumably marine environment. The Boorthanna community, however, is unusual both in its abundance and its fidelity of preservation. Moreover, it is exceptionally diverse, apparently including bacteria, filamentous, unicellular and colonial blue–green algae, and several types of unicellular and possibly colonial eukaryotes. As perhaps the most diverse and abundant of the few stromatolitic microfloras now known, the assemblage provides an unusual opportunity to investigate the relative importance of biotic and environmental factors in the development of stromatolite morphology, a matter crucial to the proposed use of stromatolites as biostratigraphic indicators[5]. In a broader context, the location of this late Precambrian microflora, midway between the major portion of the Adelaide Geosyncline to the south and the Amadeus Basin to the north, and the fact that microfossils and stromatolites occur in sediments of similar age in these two adjacent regions[4,6,7], suggest that the Boorthanna deposit could provide important evidence bearing on the difficult problem of interregional biostratigraphic correlation in the Precambrian. As for its evolutionary implications, this approximately 1,000 m.y. old microflora, roughly intermediate in geologic age and biotic composition between the Beck Spring and Bitter Springs assemblages, seems to represent a stage in biological history characterized by "modernization" of the cyanophytic flora[4], diversification of microscopic eukaryotes, and, possibly, emergence of the evolutionarily important process of eukaryotic sexuality[8]. The Boorthanna fossils should yield fresh insight into the composition and status of the early biota during this active evolutionary stage, a stage apparently transitional between the development of primitive, unicellular eukaryotes and the very late Precambrian emergence of multicellular, megascopic plants and animals.

The microflora is preserved in black, laminated cherts occurring within an unnamed dolomitic formation in the Peake and Denison Ranges of South Australia, an uplifted, northern extension of the Adelaide Geosyncline. Samples were collected near Boorthanna about 2 km east of the William Creek–Oodnadatta road, 460 km north-northwest of Port Augusta. The fossiliferous horizon is situated 893 m beneath the top of the formation and 1,233 m beneath the base of a tillite equivalent to the late Precambrian Sturt Tillite of the southern Adelaide Geosyncline. The unnamed formation is apparently correlative with the Adelaidean Skillogalee Dolomite, a correlation suggesting an age of about 1,000 m.y. for the formation[6,9].

The Boorthanna cherts are remarkably fossiliferous, commonly containing more than 10,000 microfossils cm⁻³. The fossils range from brownish amber to dark brown and can be freed from the chert by hydrofluoric acid maceration. The orientation (Fig. 1d) and great length (Fig. 1a) of the organically preserved filaments and the occurrence of the assemblage within stratiform and Collenia-type stromatolites indicate that the Boorthanna organisms constituted a mat-building microbiological community that was permineralized by silica in situ near the sediment–water interface.

The more than two dozen types of microorganisms recog-
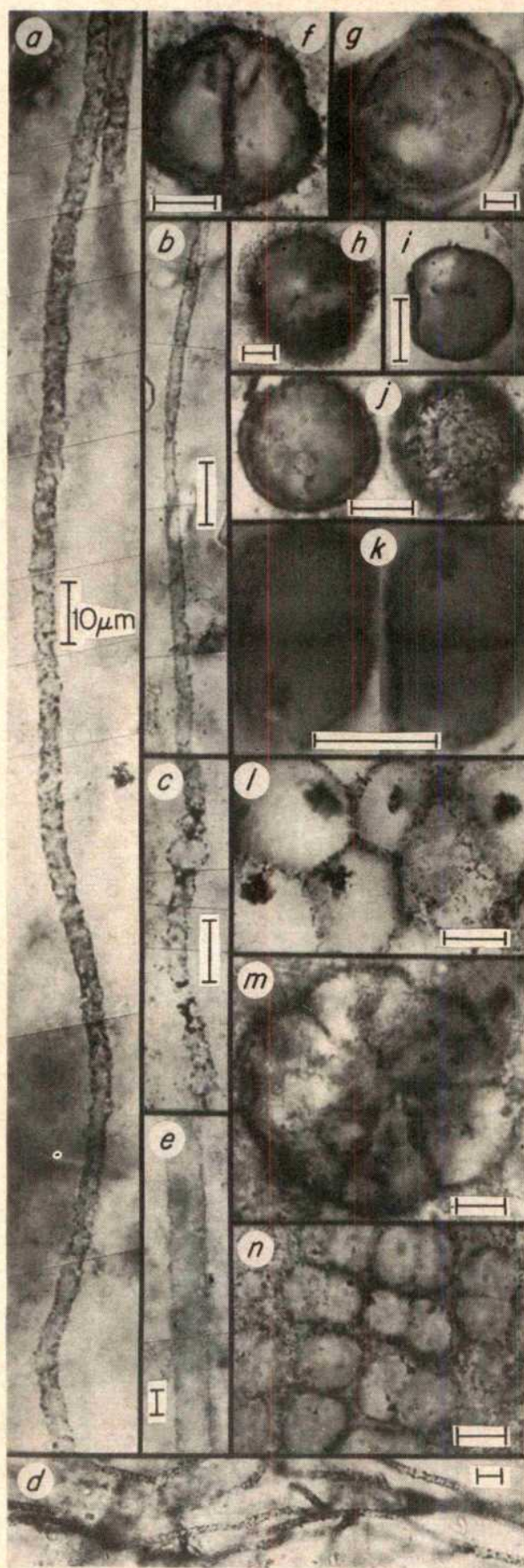
Fig. 1 Optical photomicrographs showing microfossils in thin sections of late Precambrian chert from Boorthanna, Australia. Composite photomicrographs are shown in *a–c* and *e*; specimens in *j* and *k* are shown at two focal depths; lines for scale, 10 μm.

nized in the deposit will be described formally after additional study. Here we divide the assemblage into five broad categories: cellular filaments, nonseptate filaments, solitary unicells, colonial unicells, and unicells containing organelle-like bodies.

Cellular filaments (Figs. 1*a–d*) are uniseriate, unbranched and range from 0.5 to 6 μm in diameter. The narrowest filaments are probably bacteria. Broader filaments seem comparable to nostocalean blue–green algae, a comparison strengthened by the occurrence of enlarged, intercalary, heterocyst-like cells (Fig. 1*c*).

Nonseptate filaments (Fig. 1*e*) are broad and thin-walled; like comparable forms from the Gunflint (*Animikiea*[2]) and Bitter Springs assemblages (*Siphonophycus*[4]), they seem to be empty sheaths that originally enclosed cellular blue–green algal trichomes.

Solitary unicells (Figs. 1*g–j*) range from 3 to 60 μm in diameter and have psilate or granular surfaces. Most resemble chroococcacean cyanophytes; many, however, are of uncertain affinities (for example, Fig. 1*g, j*).

Colonial unicells, morphologically quite similar to living blue–green algae, occur both in rounded aggregations (Fig. 1*m*; compare *Myxosarcina*, Pleurocapsaceae) and in tabular groupings one cell thick (Fig. 1*n*; compare *Merismopedia*, Chroococcaceae).

A large number of unicells, commonly occurring in colony-like clumps (Fig. 1*l*), contain granular, spheroidal, organic bodies that may represent preserved organelles (Fig. 1*f, k, l*). Similar organelle-like bodies occur in permineralized Phanerozoic plants[10] and in unicells of the Bitter Springs and Beck Spring assemblages. Although further investigations are needed to better define the nature of these bodies, their occurrence in the Boorthanna assemblage seems consistent with recent studies[3,4,8] apparently indicating that unicellular eukaryotes (green and red algae) were well established during the late Precambrian and suggests further that primitive eukaryotic colonies may have been extant as early as 1,000 m.y. ago.

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BOOK REVIEWS

Antarctic Earth Science

Antarctic Geology and Geophysics.
Edited by R. J. Adie. (Symposium on
Antarctic Geology and Solid Earth
Geophysics, Oslo, August 1970.) Pp.
876. (Universitetsforlaget: Oslo, 1971.)
£25.35.

THIS is the second massive international
symposium volume on Antarctic earth
science to appear within a decade. It
is a work of major importance and
must find a place on the shelves of
every geological or geophysical library
that pretends to global concern. Delving
into the volume it is a joy to see the
solemn words of the Antarctic Treaty
of 1959 once again translated into very
tangible scientific results. Although
both earth and life sciences have drawn
rich rewards from Antarctica since it
was agreed to make the continent an
international scientific laboratory,
geologists have led the way in painting
a coherent picture of the area without
regard to former national spheres of
interest. The first symposium on
Antarctic geology was held in Cape
Town in 1963. It was organized by the
Scientific Committee on Antarctic Research
of the International Council of
Scientific Unions and sponsored by the
International Union of Geological
Sciences. The 1970 symposium held
in Oslo was similarly organized and
sponsored and the proceedings of both
meetings were edited with painstaking
thoroughness by R. J. Adie. The
earlier volume weighed 2 kg and cost
£11. The present volume weighs 3 kg
and at £25.35 has unfortunately priced
itself out of the market for individual
scientists. It contains 126 papers
covering almost all the significant
advances made since science began to
loom larger than politics in Antarctica.
The Cape Town symposium was
organized with group sessions based on
separate disciplines within the earth
sciences. As a result too many
studies appeared not only geographically
but also thematically isolated. This
situation was remedied at the Oslo
meeting which was instead based on
regional studies. The evident and
rather new-found awareness among
geologists of what they stand to gain
from solid earth geophysics on a conti-

nent 99 per cent hidden beneath ice
is one of the more exciting rewards of a
regional approach. While the Cape
Town volume contained one short
paper on the "importance of Antarctica
in the hypothesis of continental drift",
almost every author in the present
volume shows an implicit if not an
explicit awareness of the significance
of his findings in a Gondwanaland context.

A number of invited review papers
on specific topics form nuclei around
which original contributions are
arranged. While the reviews are of
widely varying depth and significance,
they are authoritative and most were
up-to-date in 1971. They include
D. H. Griffiths and P. F. Barker on
marine geophysical investigations in
the Scotia Sea, R. J. Adie on recent
advances in the geology of the Antarctic
Peninsula, P. J. Barrett and others on
the Beacon Supergroup, E. H. Colbert
on Triassic tetrapods, C. Craddock and
also G. E. Grikurov and others on
tectonics, R. D. Adams on dispersion-
wave studies, A. Ya Krylov on geo-
chronology, M. G. Ravich on regional
metamorphism of the crystalline base-
ment, D. S. Soloviev on platform mag-
matic formations, P. E. Calkin and
R. L. Nichols on Quaternary studies,
G. de Q. Robin on radio-echo sound-
ing, D. E. Hayes and W. C. Pitman on
marine geophysics, and M. Girod and
J. Nougier on volcanism in the sub-
Antarctic islands. The relative interest
in problems of particular regions can
be judged from the fact that there are
twenty-four papers and two abstracts
on the Scotia Arc and Antarctic Penin-
sula, sixteen papers and one abstract on
western Antarctica, twenty-two papers
and one abstract on the Transantarctic
Mountains, thirty-seven papers on
eastern Antarctica, five papers and four
abstracts on the southern ocean, eight
papers on the sub-Antarctic islands,
and four papers on continental drift.
As with most volumes resulting from
symposia attended by the leading
figures in the subject, there is some re-
publication of material presented
earlier in journals such as *Nature* and
Science. This is perhaps justified in
that the fuller versions now presented
are in context and appear in association

with other contributions relevant to an
understanding of regional relation-
ships. Indeed so comprehensive is the
subject coverage of this and the earlier
volume that only Antarctic specialists
will need anything else on their shelves.
By the time a further symposium
volume appears, reconnaissance geology
and systematic mapping at the smaller
scales will be complete and new
chapters in the history of the continent
will be based on the results of continued
palaeomagnetic studies, much deep sea
drilling and to a lesser extent sub-ice
drilling. It is becoming increasingly
clear that although the rock surface of
almost the whole continent lies beneath
an ice sheet which in parts reaches
5,000 m in thickness, we already have
techniques that can be used to delineate
the main structural and lithological
boundaries beneath the ice. Seismic
refraction, magnetic, gravity, and radio-
echo sounding surveys, much employed
singly, now give promise of a vastly
increased yield when brought together.

In discussing a volume of 876 pages
the reviewer can only draw specific
attention to a few arbitrarily selected
topics. Recent reconnaissance mapping
appears finally to have located the
boundary between the Andean struc-
tural units of the Antarctic Peninsula
fold system and the Marie Byrd Land
ranges, the latter being interpreted by
F. A. Wade and J. R. Wilbanks as dis-
placed fragments of the eastern Antarc-
tic shield. However, the history has
been much complicated by orogenic
processes and volcanism. Some forty
volcanoes have now been identified in
Antarctica, and while most show few
signs of recent activity, Deception
Island has experienced a series of spec-
tacular eruptions in 1967, 1969, and by
coincidence also in August 1970 while
the symposium was in progress in Oslo.

There has been much recent and
detailed exploration of the Trans-
antarctic Mountains, which are now
believed to extend right across the con-
tinent as far as 73°S, 02°W in Dronning
Maud Land. D. H. Elliott and others
discuss the relationship of the Beacon
Supergroup rocks to Gondwana
sequences. Stratigraphical similarities
include Palaeozoic tillites, dark shales
overlying Palaeozoic glacial deposits,

Permian coal measures, and basalts capping the succession. The best-known palaeontological similarity is widespread *Glossopteris* flora. Until 1967 the only vertebrates recorded were Devonian and Jurassic fish remains. Tetrapod remains, which are an important part of the palaeontology of Gondwana sequences, were not found in Antarctica until December 1967. E. H. Colbert describes the exciting discovery by P. J. Barrett and others, at Coalsack Bluff near the Beardmore Glacier, of an abundant tetrapod fauna similar to the Lower Triassic *Lystrosaurus* Zone fauna of the Upper Beaufort Series, South Africa.

There is plenty of work left for the next generation. Still unsettled is the age of the start of uninterrupted continental glaciation, and whether or not the depressed continental shelf of Antarctica is due to a former greater ice loading. Until quite recently the ice sheet was regarded as a strictly Pleistocene phenomenon. Now R. H. Rutford and others conclude on the basis of glacial deposits overlain by dated volcanics that the Jones Mountains area was undergoing continental glaciation 7 million years ago, while LeMasurier suggests that an ice sheet of substantial thickness has existed continuously in western Antarctica since Eocene time. It is an intriguing subject and we can eagerly anticipate the next instalment.

The book is beautifully printed on A4 size paper, the line drawings are explicit and clear, there are several hundred good photographs and there is an index. Misprints are few by any standard. When we consider that the contributing authors came from twelve different countries (only five of them English-speaking), and that the volume was printed in English in Norway, surely the editor and all concerned deserve our congratulations and thanks for a magnificent achievement.

CHARLES SWITHINBANK

Liquid Metals

An Introduction to the Theory of Liquid Metals. By T. E. Faber. Pp. xiii+587. (Cambridge University: London, November 1972.) £12 ; $37.50.

THE study of liquid metals in a structured way began twelve years ago with the application of the pseudopotential concept, providing a theoretical framework for the subject which has remained ever since. A first international conference devoted to the properties of liquid metals was held in 1966 and a second in 1972 ; it is a measure of the continuing momentum of the subject that a third is planned for 1976. During this time several reviews have appeared and a concise monograph (March,

N. H., *Liquid Metals,* Pergamon, London, 1968) but there has been a need for a more extensive exposition. This gap is well filled by Dr Faber's book. The author has been active in the field throughout. As a result the book quite properly contains a good deal of his own original work, some of it not previously published, and is liberally sprinkled with critical comment and suggestions for further work. The level is such as to appeal particularly to experimental physicists whether new to the field or not. Mathematical arguments are kept at a relatively simple level and are fairly fully presented.

The text consists of six chapters, the first devoted to a discussion of nearly free electrons (NFE) on which the effect of the ions is calculated by perturbation methods using a pseudopotential. This is basic to the rest of the book in which the recurring theme is the extent to which an NFE model is applicable to real liquid metals. This governs in part selection of material ; liquid transition metals and liquid semiconductors are dealt with very briefly since neither can be included under an NFE umbrella.

There follow two chapters on structure and atomic motions. A discussion of the pair distribution function and its Fourier transform, the liquid structure factor, includes a critical survey of experimental data and of progress towards solution of the central problem of relating the distribution function to a pair potential. The discussion of atomic motions centres round interpretation of the diffusion coefficient, particularly the light recently thrown on the detailed nature of diffusion by molecular dynamics, and progress in the difficult business of extracting details of atomic motions from neutron scattering data.

The next two chapers return to the conduction electrons, first turning to the theoretical problem of electron eigenfunctions in disordered systems, and the experimental help we can expect from techniques such as the Compton effect. This leads the way for a discussion of electron transport, both d.c. and at optical frequencies, where the remarkable successes of the NFE model appear in profusion and discrepancies in detail even begin to be understood. The final lengthy chapter extends the theoretical ideas to a treatment of alloys and surveys the vast pool of available experimental data.

A successful innovation is the use of a prologue preparing the reader for the argument in each chapter ; this will surely be found useful and the practice should be commended to other authors. The book is furnished with a useful collection of references ; fittingly some two-thirds of them (about 500) relate to the period 1965–72 which has seen the bulk of the activity in this relatively young subject.   E. F. W. SEYMOUR

Protobiogenesis

Molecular Evolution and the Origin of Life. By Sidney W. Fox and Klaus Dose. Pp. xi+359. (W. H. Freeman: San Francisco and Reading, 1972.) $16.

THIS volume comes riding in on the crest of a great wave of new books on the origin of life, but it is very much more than just "one of the rest". Many of us have for a long time been eagerly waiting for its appearance. The authors are both distinguished practitioners of a small band of experimentalists who have been conspicuously successful in the thermal synthesis of proteinoid polypeptides. Sidney Fox has for many years championed a model in which proteinoid microspheres are regarded as "protocells", and he has shown that his microspheres, synthesized in a simulated prebiological environment, have many of the properties of Oparin's coacervates (which are unlikely to be "prebiological", as they can only be synthesized from pre-existing proteins).

The first three chapters deal briefly with the historical, cosmological and geological backgrounds. These aspects of the origins of life are common to most of the new books on the subject, but Fox and Dose have succeeded in bringing out many points of view absent from the rival volumes. Even in the historical section, where the work of A. L. Herrera receives special mention, they have succeeded in developing a distinctive philosophy. The theories of Fox and Dose are, of course, controversial. They champion thermal energy as the power for the final act of what they call "protobiogenesis", and they postulate as a site for this event a volcanic environment. In chapter 3, they consider energy sources, and make an eloquent case for seeking sources which are applied not in the atmosphere, but in lithosphere or hydrosphere. This argument will appeal to the geologist, who is used to finding that most of the energy that powers geological evolution is supplied from inside the Earth, and not from the much greater sources of radiant energy that come from outside. The Earth captures only a small part of this radiant energy, some through the agency of the weather, and the rest through the activities of living organisms which would not have been present before life had formed.

In chapter 7, they return to the theme of energy and environment and here they again enter the controversial lists, and claim that their ideas typify not reductionism, common to most biochemical reasoning, but the "constructionistic" consideration of evolving micro-systems.

The three preceding chapters deal in turn with micromolecules, with macromolecules, and with protocells. Here, on their own ground, the authors really

do communicate to their readers the excitement and enthusiasm which have been such characteristics of their work. Here, brought together for the first time, is a really authoritative and up-to-date account of the Fox hypothesis. It is illustrated with a magnificent set of micrographs, including time-lapse series, which, although many have been published before, are good to have collected together.

Four shorter chapters, on optical activity, on protein sequence, on fossils, and on extraterrestrial problems, conclude the volume. These chapters are useful in that in places the authors can bring cogent criticism to bear on the work of others, but, like the first three chapters, they lack the authority and the immediacy which are such characteristics of the central core of their work. And their enthusiasm is infectious. A special bonus comes in the last three pages. Here, in an appendix, is a recipe for home-made protocells! Readers are encouraged not only to make them for themselves, but also to feed them and watch them grow and divide!

The book is certain to be criticized, for it is much prejudiced in favour of the theories that the authors themselves have so often championed in their experiments. But there are, to my knowledge, at least four other comprehensive books on the origins of life at the moment in press, and we should very soon be able to range against each other all the rival models. Perhaps, in their enthusiasm, Fox and Dose are in danger of creating the mistaken impression that their protocells are almost already "alive". The student who defines life in functional terms may be perplexed, for in the laboratory these protocells absorb food from the environment, grow and multiply by fission. Is this not life? The answer is, of course, very firmly in the negative, for these activities are not spontaneous, they are induced by environmental changes, by (for example) increasing the pH. And in morphological and chemical terms, the differences are even greater. The membranes of protocells are chemically quite distinct from any living cell membrane, and we still await experiments in which protocells have been persuaded to incorporate nucleic acids.

Despite this danger of over-enthusiasm, the protocell hypothesis is such a vital element in the present debate on the origin of life, and it is set out so well, that the volume must surely become compulsory reading for everyone interested in the topic. The book does the publishers credit: it is well produced and reasonably priced. And it is quite the most exciting account that we yet have of what must surely be the most exciting event in the whole history of the Universe.

P. C. SYLVESTER-BRADLEY

Boundary Erosion

Meaning and Control: Essays in Social Aspects of Science and Technology. Edited by D. O. Edge and J. N. Wolfe. Pp. x + 274. (Tavistock: London, February 1973.) £4.

ARTHUR KOESTLER, I suppose, might have it that making a book of the papers presented at an international conference is like trying to provide a call girl service by post. Personal contact not being transmissible by the Gutenberg technology, how much point is there in what remains?

If the quality of individual contributions were all that mattered, this volume would pass muster without question. One is entitled, however, to look for more: the coherent development of a theme. The editors suggest that metaphor, and the social context of its use and abuse, form such a theme; but I doubt whether many readers will perceive it as such, once past the first two papers, in which first D. C. Bloor and then Edge deal explicitly with it.

Perhaps the strongest recurrent thread is the attempt to erode boundaries between science and other aspects of human endeavour. Bloor makes the point plainly in his transparently lucid attack on Oxford linguistic philosophers: it is for "boundary maintenance"—for trying to see different spheres of competence as autonomous—that he berates them. Harry Kay points out that, though in general the medium of technology is "more penetrating than any of its hardware", it has not effectively permeated our educational structure; most new machines are not being well integrated into teaching. Eric Trist traces to the dialectic between the "scientific" and the "human relations" approaches to management the newer attempts to organize the technology-people interface; "only the socio-technical whole could be effectively optimized", and principles for job design should explicitly take this into account. Frank Bechhofer's problem regarding shop-floor behaviour is similar, and F. R. Bradbury makes matters specific with regard to the chemical industry.

W. H. G. Armytage wittily traces technocracy through a century and a half. Lewis Gunn analyses the way in which MinTech, "lean and purposeful" in 1965 and concerned with the planned promotion of selected research and development (R and D) programmes, rapidly grew by accretion to become a broadly based sponsoring department for industry. Edwin Mansfield gives a useful summary of his research findings on R and D management, and Wolfe adds a note on cost escalation. R. W. Davies shows how in Soviet Russia, as in the West, there have been attempts to bring R and D closer to users. A brief but cogent paper by

Christopher Freeman deals with R and D for less developed countries.

Although it is hardly possible to deny that issues arising from the science-society relationship form just about the most important group of problems facing mankind, the point still needs making in academic circles, and it is good to see it made in a volume of such high calibre. Some of the papers have suffered from the three-year lag between conference and publication, and some of the newer areas of frontier activity like environment, pollution and conservation are barely mentioned.

F. R. JEVONS

Prime Number Problems

The Distribution of Prime Numbers: Large Sieves and Zero-Density Theorems. By M. N. Huxley. Pp x + 128. (Clarendon Press: Oxford; Oxford University Press: London, 1972.) £6.50.

ORIGINALLY, a large sieve was a result expressing in quantitative form the fact that a sufficiently dense integer sequence is well distributed in most arithmetic progressions modulo most (small enough) primes. Nowadays the name covers also a class of allied inequalities for averages of trigonometric and character sums; such inequalities have assumed in recent years increasingly sharp and comprehensive forms, and have led to significant progress in the notoriously difficult study of prime numbers. In 1967 there appeared *Multiplicative Number Theory* (Markham, Chicago) in which the late Professor H. Davenport described the early stages of these developments by ending an exposition of classical prime number theory with a simplified account of Bombieri's now well-known result on the distribution of primes in arithmetic progressions. More recently (1971) H. L. Montgomery's *Lectures on Multiplicative Number Theory* (Springer) have traced the important developments since then (most of these, incidentally, due to himself); and now Huxley's monograph takes the story almost up to the present. Dr Huxley tends to follow Davenport (to whose memory the book is dedicated) in the organization and choice of material; but he is able, of course, to give an account of much more powerful large sieve techniques and of superior results about the zeroes of ζ- and L-functions. He concludes with an account of Vinogradov's famous three primes theorem, based on Montgomery's treatment of the associated trigonometric sums, and with his own result for gaps between consecutive primes, which refines a technique of Montgomery and is currently the "world record", after many years of very slow progress. Huxley is a leading expert in the field, and he shows this in many ways in the course of the book. One of

the ways, unfortunately, is an excessively condensed presentation which, together with some inaccuracies and inadequate references to the ramifications of the various topics introduced, diminishes the value of his book. Individual chapters are heralded by thoughts from Winnie the Pooh, and there are corners of the world where these will be found harder to understand than the chapters themselves. Although workers in the field will be glad to have the latest developments available so soon, they will find reading the book very difficult, and they may well be discouraged from purchasing it at such an outrageously high price.   H. HALBERSTAM

Molecular Spectroscopy

Molecular Spectroscopy: Modern Research. Edited by K. Narahari Rao and C. Weldon Mathews. Pp. xiii+ 422. (Academic: New York and London, May 1972.) $25.

THIS volume was issued to commemorate the twenty-fifth anniversary of the Columbus Symposium on Molecular Structure and Spectroscopy, a symposium held annually in the United States at the Ohio State University. The book contains a mixture of review articles, invited talks from the 1970 symposium, and data compilations, though these three categories are not mutually exclusive. Because the material in this volume is so heterogeneous, prospective readers wishing to decide how many articles are closely· allied to their own research interests have no recourse but to scan a list of contents. Such a list, with somewhat abbreviated titles, is given in the next paragraph.

One would probably classify as review articles the sections on: microwave spectroscopy (Morino and Saito), rotational levels of free radicals (Carrington), high-resolution IR of planetary atmospheres (Fox), vibration-rotation structure in asymmetric- and symmetric-tops (Mills), electronic spectroscopy of polyatomics (Innes), nuclear hyperfine structure in diatomic electronic spectra (Dunn), IR and UV matrix studies of free radicals and molecular ions (Milligan and Jacox), Fourier spectroscopy (Sanderson), grille spectrometers (Moret-Bailly), and large IR plane gratings (Rao). Written versions of 1970 invited talks include the sections on: Lamb-dip hyperfine spectrum of I_2 (Bunker), rotational energy transfer from MW line broadening (Boggs), rotational spectra of molecules with two internal degrees of freedom (Dreizler), interstellar molecules (Rank), rotational line strengths: the $O_2^+ b^4\Sigma_g^- - a^4\Pi_u$ system (Zare) energy transfer research in I_2 (Steinfeld), and biprotonic phototautomerism, excimer

formation, and proton tunnelling in DNA (Kasha, Horowitz, and El-Bayoumi). Finally, the data compilations include: molecular IR laser emissions (Rao and Mantz), and twelve tables of physical constants, conversion factors, wavelength standards, and so on.

There is no question that each of these contributions represents, in its own way, an interesting, enlightening and useful treatment of selected subject matter by a recognized authority in the field. In my own laboratory, those who read the volume all found one or more particularly valuable articles. On the other hand, readers also found article(s) they felt might well have been omitted. Unfortunately, there was no general agreement in selecting individual articles for praise or criticism.

The most attractive general feature of the book to me is the set of excellent longer review articles with large numbers of reference citations, which will be useful for the next several years to anyone beginning work on a problem in one of the areas covered. The line lists and tabulations of constants are also convenient, though they are often accessible elsewhere in the literature.

Perhaps the most severe criticism of the book which comes to mind concerns not the individual articles themselves, but rather the collection as a whole. I am not in favour of the proliferation of random review volumes and/or conference proceedings such as this, which offend one's sense of order and complicate one's literature searches by not fitting neatly into the format of already existing periodic scientific communication channels.   JON T. HOUGEN

Oral Biology

The Marmoset Periodontium in Health and Disease. By B. M. Levy, D. Dreisen and S. Bernick. Pp. 89. (S. Karger: Basel, London and New York, 1972.) 39 Sw. francs; £4.30; $10.

THIS, the first volume in a series entitled *Monographs in Oral Science,* contains no editorial statement about the scope and aim of the series; nevertheless, the need for animal models to study prevalent dental disease such as gingivitis and pyorrhoea is sufficient reason for this topic to be chosen to initiate the series.

The marmoset, or "manikin", is susceptible to periodontal disease, especially in captivity. Its small size, near-human dentition, and ready availability have made it a most suitable subject for the intensive study of periodontal biology and the reaction of dental supporting tissues to environmental change and injury.

The monograph, in two principal parts, begins with a detailed descrip-

tion of the development of deciduous and permanent dentitions of the marmoset, the structure of the adult periodontium, and its change with increasing age. The text is crisp, and the black-and-white illustrations comprehensive and clear. A monograph on comparative anatomy gains immeasurably by frequent, apposite references to the human situation. That this booklet generally fails to draw these comparisons diminishes its value as a reference work. The deficiency is remedied in the second part devoted to the initiation and extension of periodontal disease. In discussing the role of the external and internal oral environment in the ecology of the periodontium, convincing parallels are drawn between the human and the non-human primate model.

The role of bacteria, viruses, dental plaque and saliva, all key factors in the external environment, has been examined and compared with their suspected role in periodontal disease in man. Dietary changes, vitamin deficiency, and endocrine imbalance have all been employed as tools to influence the internal environment of the periodontium. Results from these valuable studies in the marmoset support Frenkel's contention that "Spontaneous models are most useful to provide inductive hypotheses concerning disease processes in man". If the contents of this slim volume are an indication of things to come, then the series will be of the utmost significance to oral biologists.   D. E. POSWILLO

Human Neurophysiology

Neurophysiology Studied in Man. Edited by G. G. Somjen. (Proceedings of a Symposium held in Paris -at the Faculté des Sciences, July 1972.) Pp. xi+487. (Excerpta Medica: Amsterdam, 1972.) Dfl. 108; $33.75.

THIS symposium, with about ninety contributors, contains as its most distinctive part a great many observations relevant to normal neurophysiology that were made as incidents in treating patients, and could not have been made without the opportunities provided by therapeutic or diagnostic procedures. Papers within this field make up nearly half of the book, and cover the field so widely that the book is quite a good guide to its literature.

Another large part of the book (also nearly half) describes experiments on normal human volunteers. This field is too large for there to be any possibility of covering it in half a symposium, and papers within it look almost randomly selected. They include, I think, the best and the worst in the whole symposium.

Two or three papers are primarily about diseases, and hardly touch neurophysiology.   G. S. BRINDLEY

CORRESPONDENCE

HeLa

SIR,—I would like to thank all those who responded to my letter (*Nature,* **242**, 144; 1973) especially Dr Howard W. Jones, jun., of the Johns Hopkins Hospital. He drew my attention to a publication[1] which leaves no doubt that HeLa cells were named after Henrietta Lacks. The mother of five children, she died less than eight months after her tumour was diagnosed at the age of thirty-one. Others have sought to correct my grammar; to one of these I would point out that the feminine noun "negress" was deliberately avoided as it is known to be offensive to some, and to another that it is just an accepted anomaly of our language that a person's name (singular) is invariably two or more names (plural). I was amused by the suggestion that Gey named HeLa after a favourite film star but it does not fit the facts — Hedy Lamarr is a caucasienne so she, along with Helen Lane, Helga Larsen, Heather Langtree and other unlucky guesses, must now withdraw as gracefully as they can.

Yours faithfully,

J. DOUGLAS

Department of Applied Biology,
Brunel University,
Kingston Lane, Uxbridge

[1] Jones, H. W., McKusick, V. A., Harper, P. S., and Kuang-Dong Wuu, *Obstet. Gynecol.,* **38**, 945 (1971).

Scientists' Careers

SIR,—It is a pleasure to notice as a common strand running through your excellent group of articles on "Careers for Scientists" (*Nature,* **242**, 375; 1973) the recognition of science courses as an education fitting the graduate for an almost unlimited range of work rather than as a narrow vocational training. Naturally somebody of my persuasion would have liked to see the point emphasized even more, would have liked to see it everywhere accepted with joy rather than as, here and there, with a somewhat regretful attitude, would have liked all the articles to echo Dainton's admonition to the universities to adapt their teaching accordingly. But, above all, employers must more generally look at scientists not as a unique species fitted only for laboratory jobs, but as educated people who must be considered with all others for every task requiring intellectual ability.

It is, however, not only at the start of his career that the scientist should look beyond the confines of the laboratory bench job. An increased mobility of experienced research scientists, just as of raw graduates, would benefit them, their employers, society at large, and the graduates who follow them. My Task Force is trying to assist this mobility through arranging interchanges so that the scientist can experience a new kind of work without having to give up his earlier career irrevocably.

Yours faithfully,

HERMANN BONDI

Task Force on Interchange of Scientists,
Civil Service Department,
Whitehall, SW1

Looting Art Treasures

SIR, — As an Italian-born American citizen I feel that I belong to the looting and the looted party in the case of the Greek vase bought by the Metropolitan Museum in New York from a dealer resident in Rome (*Nature,* **242**, 155; 1973). From this vantage point I am not so sure that the singling out of the Metropolitan Museum is wholly justified. It seems to me that all nations at one time or another have practised looting of art objects on a grand scale. From the Bronze Horse of the Pala D'oro in St Mark to the tapestries of the Duke of Burgundy in Berne, and from Lord Elgin's marbles to the illuminated manuscript in the Bibliothèque Nationale Française, it seems to me the looting has been the rule rather than the exception for several centuries. (I must say that if I have omitted other nations it is not because they are innocent, but simply that their looting has been inferior in quality rather than quantity.)

The only trouble with the Metropolitan Museum is that they arrive with a wolf's hunger to a banquet that is already over; or, to put it in biblical terms "whosoever is without sin, let him cast the first stones" (or should I say "the first marbles"?).

Yours faithfully,

RENATO BASERGA

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Obituary

Academician
A. N. Tupolev

ACADEMICIAN ANDREI NIKOLAEVICH TUPOLEV, the famous Russian aircraft designer, died on December 23, 1972, after a long illness.

Tupolev, who was born on November 10, 1888, the son of a notary, was educated at the *gymnasium* in Tver' and then at the Moscow Higher Technical Institute, where he studied under N. E. Zhukovskii, the aviation pioneer.

In 1918, after graduating, Tupolev assisted Zhukovskii in the organization of the Central Institute of Aerohydro-dynamics, becoming one of its Deputy Directors, and, in 1922, Director of its Design Bureau. From then on, Tupolev became increasingly the most prominent figure in the Soviet aviation industry, designing in all some 120 types of aircraft.

During the 1920s he carried out extensive research into the use of duralumin in aircraft construction, and is widely regarded as one of the pioneers of all-metal aircraft. In 1934 he constructed an experimental eight-engine pasenger aircraft, the "Maxim Gorky" with a wing span of some 65 m and weighing 40 tons. This aircraft made a number of successful test flights but crashed in 1935, an accompanying fighter plane being, apparently, responsible for the disaster.

In 1936, Tupolev visited Germany and the USA to study foreign aircraft construction. Shortly after his return to Russia, during the Stalinist purges, he was accused of "divulging aviation secrets" and sentenced to forced labour. During his imprisonment he designed a twin-engined divebomber, the Tu-2 which was put into production in 1939 and formed an important part of the Soviet air arm during World War II. Shortly after designing this aircraft,

Tupolev was released and returned to work at the Design Bureau of the Central Institute of Aerohydrodynamics, where he remained for the rest of his working life, gradually acquiring a great number of titles and awards, including Member of the Academy of Sciences of the USSR (1953), Designer General to the USSR Ministry of the Aviation Industry (1965), three Stalin Prizes (now State Prizes), one Lenin Prize, the Order of Lenin (8 times), the Order of the Red Banner of Labour (twice), the order of the Red Star (twice) and the title of Hero of Socialist Labour (twice), this last being the highest Soviet civilian award.

Among the most notable aircraft designed by Tupolev during the course of his long career were the single-engined ANT–25 which in 1937 made the first non-stop trans-polar flight from the Soviet Union to the USA, the four-engined ANT–6 which landed the personnel of the Soviet North Pole expedition in 1937, the first civil passenger turbo-jet, the Tu-104, and the supersonic passenger aircraft, the Tu-144, which is expected to go into service in 1975.

Andrei Nikolaevich Tupolev, who gave his name to the Tu-series of aircraft, is succeeded as head of the design team by his son, Aleksei Andreevich, who, it is understood, will be in charge of final tests and modifications to the Tu-144.

Announcements

University News

Dr **Peter Watt**, St Mary's Hospital, Medical School, has been appointed to the Chair of Microbiology at the University of Southampton as from October 1, 1973.

Miscellaneous

Professor **Sir Ernst Chain**, Department of Biochemistry, Imperial College, has been awarded the Grand Decoration of Honour in Gold for his services to the Republic of Austria.

Dr **J. H. Baxendale**, Department of Chemistry, University of Manchester, has been awarded the Weiss Medal for his contributions to radiation research.

The following have been awarded the **Linnean Society Gold Medal**: Professor **G. L. Stebbins**, University of California, and **Professor J. Z. Young**, University College London.

Dr **Ursula K. Duncan** has been awarded the H. H. Bloomer award by the Linnean Society of London.

Mr **N. L. Falcon** has been awarded the Founder's Medal of the Royal Geographical Society.

Professor **E. H. Thompson**, University College London, has been awarded the Patron's Medal of the Royal Geographical Society.

Dr **A. H. Chilver**, Cranfield Institute of Technology, has been appointed chairman of the committee of Education and Training at the Department of Trade and Industry.

Mr **H. Surtees**, Easams Limited, has been appointed chairman of the committee of Materials Handling at the Department of Trade and Industry.

Mr **N. Sheperd**, Dept of Trade and Industry, has been appointed chairman of the committee of Information and Publicity at the Department of Trade and Industry.

Dr **Sidney Passman**, US National Science Foundation, has been appointed director of the division of Scientific Research and Higher Education at Unesco in Paris.

Errata

IN the article "Comments on the Isolation, Identification and Synthesis of a Specific-Behaviour-Inducing Brain Peptide" by Avram Goldstein (*Nature*, **242**, 60; 1973) the first sentence of paragraph 2 should read: "The long controversy over the claims for transfer of learned behaviours was reviewed by W. W. Stewart[2] that involved a rebuttal by Ungar *et al.*".

IN the article "Isolation of the Islets of Langerhans for Transplantation" by D. R. Thomas, M. Fox and A. A. Grieve (*Nature*, **242**, 258; 1973) paragraph 1, line 5 and following, should read: "One of the major problems has been to overcome pancreatic exocrine digestion. Pancreatic duct ligation ("Banting pancreas") before transplantation has been performed with this in view."

Reports and Publications

not included in the Monthly Books Supplement

Great Britain and Ireland

Bulletin of the British Museum (Natural History). Entomology. Vol. 27, No. 4: Revisional Notes on African *Charaxes* (Lepidoptera: Numphalidae), Part VIII. By V. G. L. van Someren. Pp. 215–264+12 plates. (London: British Museum (Natural History), 1972.) £5.   [12
Agricultural Research Council. Meat Research Institute Annual Report 1971–72. Pp. 105. (London: Agricultural Research Council, 1973. Obtainable from HMSO.) £1.40 net.   [12
New Developments in Manufacture and Use of Liquid Fertilisers. By A. V. Slack and F. P. Achorn. Pp. 51. (London: The Fertiliser Society, 1973.) [12
Commonwealth Forest Institute. Paper No. 45: The Planning and Evaluation of Forestry Projects. By G. R. Watt. Edited by J. J. MacGregor. Pp. xii+83. (Oxford: Commonwealth Forestry Institute, University of Oxford, 1973.) £2 (postage 8p).   [12
The Medical Research Council of Ireland. Annual Report for the year ended December 31, 1971. Pp. 100. (Dublin: The Medical Research Council of Ireland, 9 Clyde Road, 1973.) 25p.   [22
Journal of Environmental Management, Vol. 1, No. 1, January 1973. Pp. 1–84. Published quarterly. Vol. 1, 1973: UK £6.60, overseas £7.60. (London and New York: Academic Press, Inc., 1973.)   [22

The Scramble for Petroleum

PRESIDENT NIXON'S long-awaited message on energy, sent to Congress last week, appears to be principally a holding operation. It is certainly not the radical reappraisal of the American energy economy which had been looked for. The immediate need, apparent for the past three years, is to increase the availability of petroleum and its products. Plainly it will help with immediate problems that the import quota system on imported petroleums should be replaced by a complicated system of tariffs, the full economic effects of which will not be felt until 1975. If American importers can find the ships and lay their hands on supplies of crude oil from the Middle East, they will at least be able to ensure that refineries in the United States operate at full capacity in the months ahead. And two or three years from now, American competition for Middle East oil will be more substantial—the proposed levy of 21 cents on each barrel of imported crude oil is unlikely to cut back the import programme to a large extent, especially because the steps which are intended to stimulate domestic petroleum production are unlikely to yield their principal benefits quickly. What this implies is that the world as a whole must reconcile itself to increased competition from the United States on the world petroleum market, a development most likely to be welcomed by the OPEC countries. The policy of "Drain America First" will bring results only in the later years of this decade and in the 1980s.

It goes without saying that the steps which President Nixon has now taken to increase production of petroleum in the United States are sensible. It is, of course, anomalous that the country which consumes the lion's share of the world's production of petroleum should, in the past decade, have followed policies which only exacerbate its own predicament. The notion that the Federal Power Commission should in future be less zealous in restricting the price at which natural gas is sold is especially important—in the past few years, the pegging of prices at uneconomic levels has done more harm than physical shortages. On offshore drilling and the building of the Alaska pipeline, the President has been forced, rather late in the day, to resolve the conflict which has grown up between environmental considerations and the rising demand for petroleum in the United States—in many ways he could have said where the federal government stands much earlier. The Alaskan pipeline has been dealt with especially timorously—it has been plain for the best part of two years that legal battles in the courts could only create such confusion and delay that new legislation would be necessary. It is inexcusable that the Administration should have shillyshallied for the past year when the prospect of a petroleum shortage was steadily worsening.

And even now the Administration has not faced up to the underlying problem of petroleum in the United States—that most petroleum products are at present sold at prices which are uneconomically low and which offer few of the incentives to more economical use which the circumstances require. Gasoline prices in the United States are only a half of those now current in Western Europe. Both natural gas and heating oil are comparatively cheap, with the results that incentives for thermal efficiency are diminished. Yet there is an obvious need that the pace of consumption of petroleum in the United States should be brought much more closely into line with the pace at which supplies are likely to increase in the next few years, which implies that Americans should be required to think twice about the ways in which they consume gasoline in particular and petroleum products of all kinds as well. To be sure, the consequences would be considerable—the gay abandon with which motor cars are at present used would be diminished. But that is one of the realities of life with which the United States must sooner or later come to terms. The sooner the better, if demand is to be sensibly matched against supply.

Fun and Games with GNP

ONE of the strange manifestations of the environmental disputes of the past few years is the way in which the Gross National Product has come in for criticism and unwarrantable reinterpretation. Some years ago, Professor Kenneth Boulding, in a book review with the same title as this leading article, quite legitimately pointed out that the Gross National Product, which is a perfectly proper statistic to use as a measure of a nation's economic activity, is not necessarily a measure of a nation's well-being or of the happiness of its people. From this, of course, no classical economist will dissent. One of Boulding's own illustrations of the point is the case of a man who employs a housekeeper whom he later marries. To begin with, he pays her a salary which is added to the GNP. But the housekeeping money which she later receives does not, by convention, count. In other words, the transition to the married state is accompanied by a reduction of the GNP, but who would not agree that the sum of human happiness has most probably been increased? Classical economists and others would also, of course, agree that while the GNP may be a useful measure of the comparative economic activities of two very similar countries, Britain and France for example, there is not much value in using it as a yardstick for comparison between countries as dissimilar as, say, Britain and India. The value of the statistic to the economists is that it establishes an algebraic identity between two different sets of variables—the total value of goods and services produced in any year (imports and exports assumed negligible) and the sum of personal expenditure, public expenditure and saving. It is no surprise that the

Gross National Product has been and will continue to be a necessary tool in the formulation of policies intended to relate, for example, a government's budget deficit to the rate of industrial output.

From this point of view, the crusade of the environmentalists against the Gross National Product is as absurd as would have been a crusade against the Gibbs Free Energy on the grounds that it does not provide a simple rule for showing how energy will flow from one system to another except when the characteristics of the second system are defined. To be sure, there are now, as there always have been, pertinent questions to ask about the kinds of economic activities most likely to benefit a particular community, and it does not always follow that the changes most likely to lead to the rapid growth of GNP will be the most desirable or the most desired. It remains something of a puzzle to know why the critics of the GNP as a measure of human happiness should be so anxious to define other yardsticks that might be more suitable. This, at least, is now a popular sport. No doubt it will be with us for a long time to come.

The article by Mr R. E. Overbury on page 561 of this issue of *Nature,* which has been published at his request against the advice of qualified referees and without revision in the light of constructive editorial suggestions, is a typical example of the new genre. The interest of Mr Overbury's article, and the point which needs developing, is the usefulness of matrix methods (with which economists have long since been familiar) for the analysis of how different components of the economic activity of a country can be related to the input of primary material. The essence of his error is the curiously subjective way in which the Gross National Product itself is redefined as the sum of gross consumption—equated with the "real cost", whatever that may be, to society—and the rest, supposed to be used in "improving the state of society". By any test, this is a thoroughly subjective definition. Mr Overbury himself admits that his distinction between good and bad is somewhat arbitrary. He could have gone further and said that it is nonsensical. As far as can be told, his objective is to distinguish those activities which consume resources and which are therefore to be discouraged in a closed society and those which improve the state of society and which are assumed, for no particular reason, to be compatible with a closed environment. But there are obvious flaws in this argument. Education, for example, supposedly in Mr Overbury's sense one of the economic activities that lead to the improvement of society, is a considerable consumer of resources in exactly the same way as other less well favoured kinds of economic activities. For even if teachers who stand in front of classrooms make only modest demands on resources, the structures in which they teach are a drain on raw materials while the salaries which they are paid, like the salaries which go to the growing (but still inadequate) armies of ancillary workers in education, are eventually spent on exactly the kind of consumption which Mr Overbury labels bad. In short, his arguments for a reinterpretation of Gross National Product are both unnecessary and misleading.

A second flaw in the argument that Mr Overbury presents is the implicit assumption that the time has come to regard the economic system of the world as a whole as a closed system. This is manifestly untrue. For one thing, a great deal of agricultural production is a direct consequence of the conversion of solar energy into edible chemicals. For another, even though it is in some literal sense true that the Earth is finite, the extraction of raw materials is at present based on such a limited technology that it consists of almost literally scratching the surface of the Earth. For example, although uranium mining at present entails essentially conventional mining operations, the time may yet come when extraction from seawater will enormously increase this natural resource. To point this out does not imply that a consideration of closed economic systems has no value, but, like all essentially academic exercises, its object should be to identify those parts of the problem likely to have a bearing on the real world. To claim more, as Mr Overbury has done, is to confuse.

100 Years Ago
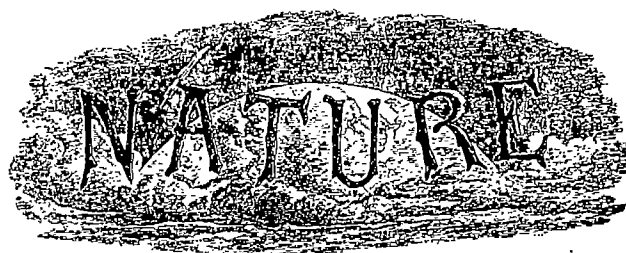
East India Museum

ALLOW me to make yet another suggestion (in addition to those of P.L.S. and Prof. Newton), with regard to the disposal of the natural history collections at the India House. It seems to me to be one of the greatest popular delusions, that specimens of natural history necessarily require lofty halls and spacious galleries for their preservation and exhibition in a useful manner. I hold, on the contrary, that, with few exceptions, they far better serve educational and scientific purposes when arranged in ordinary apartments. All the scientific work in the British Museum is done in small rooms; and the palatial galleries with their crowded myriads of specimens and miles of glass cases, however instructive they may be (or might be made) to the public, are a positive hindrance to scientific work. I am very much mistaken if all the India House natural history collections might not be suitably placed in two or three ordinary sitting rooms, and so arranged in cabinets and boxes as to be far more convenient for reference and study than they have ever been. The rent of a moderate-sized house in an airy situation, say 250*l.* with an equal sum for the salary of an efficient Curator, and a small grant for cabinets and the necessary books of reference, is all the expense required to make this interesting collection completely accessible to all who wish to consult it. Every one interested in Indian natural history would then visit it. It would again receive gifts of collections from travellers, Indian Officers, and other persons interested in the natural history of the East; and its increase in value from this source alone might go far towards furnishing a tangible equivalent for the expense incurred, while it would certainly render the collection a better representation of the Indian fauna than it is at present, and more worthy of a place, at some future time, in the proposed grand Indian Museum.

Such a modest establishment would also, I believe, do much good by showing at how small an expense a really useful scientific museum may be kept up, and would thus encourage the formation of local museums in cases where 20,000*l.* or 30,000*l.* cannot be raised for a building. It would not, of course, be a show museum for the uneducated public to wander and gaze in; —the British Museum serves that purpose. But it would prove greatly superior to any such mere exhibition, as a means of furnishing definite information on Indian zoology, and enabling any intelligent inquirer to obtain some idea of the many wonderful and beautiful forms of life which characterise, what is at once the smallest and the richest in proportion to its extent, of the great zoological regions of the globe.

ALFRED R. WALLACE

From Nature, **8,** 5, *May* 1, 1873.

OLD WORLD

ESRO Chooses Two New Scientific Satellites

THE European Space Research Organization has decided to fly two new scientific satellites in 1977 and 1979. The final choice has fallen on HELOS (Highly Eccentric Lunar Occultation Satellite) which will examine X-ray sources, and ISEPS (International Sun–Earth Physics Satellites Programme) one of a pair of satellites designed to study the earth's magnetosphere and the adjacent boundaries of interplanetary space. The second satellite of the pair will be launched by NASA.

The decision to launch these two satellites commits ESRO to an expenditure of 63 million units of account (about £19 million) on HELOS and 23.4 million units of account (about £7 million) on ISEPS, which is also known as the mother–daughter satellite.

It was originally thought that only one out of the three projects up for consideration by the ESRO council would be chosen (see *Nature*, **242**, 79, 1973). The unsuccessful project was the Venus orbiter, designed to investigate the atmosphere and surface of Venus, and this has gone by the board chiefly because NASA, which was to launch the satellite and provide some of the experiments, has no provision in its 1973–74 budget for the satellite, and ESRO was not prepared to go ahead alone, even though the council was satisfied that the project was scientifically sound. Without NASA's participation the need to buy a launcher and provide all the experiments and ground tracking facilities would have raised the cost considerably for ESRO. Nonetheless the project will probably be represented when ESRO chooses its next set of satellites in 1976. There is another launch window in 1980 (originally it was hoped to launch in 1978) and if NASA is interested the project may go ahead then.

Meanwhile cooperative plans go ahead to launch the mother–daughter satellites in 1977. This project, which consists of two satellites launched on the same Thor-Delta rocket, will be tied in with NASA's heliocentric satellite project to provide detailed information about the way in which the solar wind affects the magnetosphere of the Earth. The heliocentric satellite will monitor the solar wind, while the two ESRO satellites, in different orbits in the magnetosphere, report changes in the radiation belts, the magnetopause (the boundary between the Earth's magnetosphere and the solar wind flowing past) and the bow shock and tail produced by the movement of the magnetic Earth
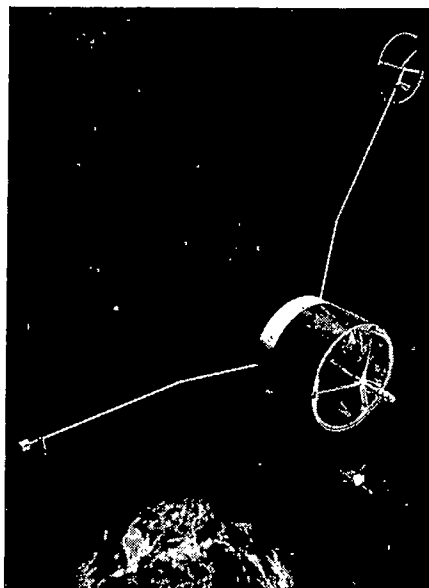
The daughter half of the joint ESRO and NASA mother–daughter project.

through the charged solar wind.

The HELOS project, although entirely independent of any other project, provides the logical and much needed next step in the development of X-ray astronomy. Because of its highly eccentric orbit, the satellite will "see" very many sources occulted by the Moon. Accurate timing of the occultations provides the most accurate measurements of the positions of these sources that is possible from X-ray observations alone. These in turn should lead to identifications with optical and radio sources—at present more than 200 discrete X-ray sources are known but only a handful have been identified with known astronomical objects. Hopefully, this sort of identification will help to resolve some of the problems of X-ray stars (are they associated with black holes, for example). The satellite also has the ability to study variable sources for several hours at a time from above the interference of the radiation belt.

EUROPE

Needed Collaboration

SLOW but sure progress is being made towards setting up a European Science Foundation. In Munich on April 13 and 14 representatives of national science organizations in ten countries in western Europe — Britain, France, Austria, Ireland, Italy, Netherlands, Spain, Sweden, Switzerland, and Germany—met for the second time in five months to discuss the possibilities and difficulties of such a venture.

The first meeting was held at the Royal Society last December when the European Economic Commission's proposals for a common scientific, technological and industrial policy, published as *Objectives and Instruments of a Common Policy for Scientific Research and Technological Development*, was discussed. But the conference, last December, felt strongly that any common European Science Foundation should be a western European organization and not restricted to countries within the EEC. A similar feeling was prevalent at Munich.

But still no decision has been made as to what form European cooperation in fundamental research should take in the coming years. Yet another meeting is planned to consider the fields in which fundamental research should be intensified and what form of organization might be suitable. This meeting will take place in Paris at the end of Sep-

tember. In the meantime, however, the representatives of the national research councils and academies who attended the Munich meeting are considering the most appropriate form for the foundation. In particular, before such a foundation is set up, the relationship of the foundation to the already existent European collaborative projects must be determined. For example, the medical research councils of Europe already meet regularly and the European Scientific Exchange programme ensures contact between the Royal Society and other academies.

But how will the European Scientific Foundation be financed if agreement is reached next September on setting it up? Dr R. W. J. Keay, of the Royal Society said this week that it is hoped that the research councils and the academies will contribute part of their budgets towards the foundation but that some support is expected from the European Commission as well.

Even if no decisions emerged from the Munich meeting it at least showed that the thinking within the European Commission is not too divergent from that of European scientists. The fear expressed at the meeting in London in December was that the EEC would impose a European Science Foundation on European scientists possibly against their wills. But the presence of Professor R. Dahrendorf, Commissioner with responsibility for Science and Technology, at Munich, showed that a common objective can be achieved.

ANGLO–SOVIET SCIENCE

Hope for the Future?

A CEMENTING of relations between Britain and the Soviet Union in the applied scientific, technological, trade and economic fields took place in Moscow last week.

This was at the second meeting of the permanent United Kingdom/USSR inter-governmental commission (Joint Commission) for cooperation in these fields, the first of which was held in January 1971. After that meeting, enthusiasm for the aims of the Joint Commission waned, but last October a ten day visit to Britain by a delegation from the Soviet State Committee for Science and Technology put much needed life into Soviet–British relations in science and technology.

The British delegation to Moscow was led by Mr Peter Walker, Secretary of State for Trade and Industry, while the Soviet group at the meeting was led by Academician V. A. Kirillin.

The Joint British/Soviet Commission called for a greater cooperation between scientific research organizations and companies in the two nations.

But the *communiqué* released from Moscow after the meetings last week is more a statement of intent than a plan for action. It is clear that both sides expressed willingness to cooperate and exchange ideas, but the driving force to get cooperative ventures off the ground must come from the scientists and from industry. The *communiqué* makes special mention of collaboration that already exists—for example, in plasma physics, where scientists from the Culham Laboratory of the United Kingdom Atomic Energy Authority are collaborating with their Soviet counterparts and also in radio astronomy.

The new lease of life given to the Joint Commission by last week's meeting means that both Britain and the United States now have an effective machinery for cooperation with the Soviet Union. An agreement was signed between the United States and the Soviet Union in May 1972 effectively setting up a committee very similar to the one that met last week (see *Nature*, **237**, 247 ; 1972).

But how does cooperation work from the British side? Before the Joint Commission was set up in January 1971 there were in existence several working groups on specific technological and scientific problems which were set up in 1967–68 under the auspices of the Confederation of British Industry and the Soviet State Committee. One of the articles of the agreement which set up these committees stated that there should be exchange visits between applied scientists and technologists in Britain and the Soviet Union. This was designed to complement the already existing, and active, exchange programme between the Royal Society and the Soviet Academy, which chiefly caters for pure scientists. But from the British point of view the exchanges under the 1967–68 scheme have not been completely successful. Only a few exchanges have taken place and the British people involved have generally had to pay their own way to Moscow, although during their stay they are sponsored by colleagues in the Soviet Union. The few Soviet scientists to come to Britain have done so on a similar basis.

It is, however, cheerful to note that the next meeting of the Joint Commission has already been set for London—sometime in 1974.

EDUCATION

Sir Brian Defends

SIR BRIAN FLOWERS, chairman of the Science Research Council, said last week that his council "regarded it as a matter of national importance to further the engineering profession", as little has been done in the training of engineers during the past 20 years. Giving evidence to the Select Committee on Finance in Education and Arts, Sir Brian said that the SRC has attempted to rectify the situation by using "its most powerful weapon—its money".

The universities pay for about half the research studentships in the sciences. The SRC's policy of allocating more grants to applied research was, at first, hindered by the universities allocating more grants to the pure sciences. Now, according to Sir Brian, the situation has changed and considerably more emphasis is being placed on the applied sciences.

This bias towards applied science raised the question as to whether a separate Technical Research Council should be formed—possibly as a branch of the SRC. Sir Brian insisted that "both pure and applied science would suffer" if the SRC was subdivided.

Little information is available about employment of higher degree graduates, but both the select committee and the SRC agreed that better liaison between universities and industry is necessary to ensure that worthwhile research projects are financed.

Sir Brian hotly defended the awarding of fellowship grants, and he spurned the suggestion that these fellowships were just another form of unemployment, saying that they were "a subsidy to real and lasting excellence". He pointed out that postdoctoral grants are only awarded to a very small proportion of PhDs and their duration is for two years only. Their purpose is to allow a brilliant and original researcher to carry on his project unhindered by any outside pressure.

INDIAN SCIENCE

Concern over Quality

from a Correspondent

UNEMPLOYMENT among scientists is as much, if not more, of a problem in India than it is in Britain and North America. There were five times more scientists unemployed in India in 1972 than there were in 1967, whereas unemployed arts and humanities graduates were 3.5 times more numerous in 1972 than they were five years earlier. But twice as many degrees are awarded in the arts than are awarded in the sciences each year.

In 1966–67, 45.5 per cent of the students who enrolled at Indian universities did so to take degrees in scientific and technological subjects. But the percentage has dropped every year since then and in 1970–71 it was as low as 41.4 per cent of the total enrolment.

This is symptomatic of the state of science in India, which has been in the doldrums in recent years in spite of a massive increase in support for scientific research from R1,300 million in 1967–68 to R2,140 million in 1971–72. There is deep concern about this, although ambitious plans are being formulated by scientific groups within India to use science and technology in order to eradicate poverty. At present several Indian scientists hold the rank of secretaries to the government and a phase of evaluation and consolidation in science is taking place.

But there is widespread concern about the quality of the publications of Indian scientists. This concern is not lifted by the results of a survey, carried out by Professor Rais Ahmed of the Indian University Grants Commission on publications of scientists working in India in the fields of spectroscopy, nuclear physics, electronics and solid state physics. The survey shows that in 1969, for example, 181 Indian scientists were cited in physics abstracts journals as having produced papers in spectroscopy, but in 1971 only 95 were cited. But in the same period the number of names of foreign scientists working in India who had published papers in spectroscopy increased from 100 to 162. A similar decrease in the numbers of publications by Indian born scientists and increase by foreign scientists was recorded in most of the other fields investigated. The important question, as far as the future of Indian science is concerned, is whether the drop in output is due to an overall decrease in the number of papers published or whether it is due to a widening gap between the standard of science as practised in India and the standard of science elsewhere.

NEW WORLD

Nixon Unveils His Energy Policy

by our Washington Correspondent

PRESIDENT Nixon did what was expected of him last week by lifting restrictions on import of oil into the United States, proposing an end to regulations of the price of natural gas and urging swift exploitation of oil and gas deposits which lie under the outer continental shelf. The actions and proposals were outlined in his long overdue message on energy policy, which was finally unveiled last week and which shared the front pages with the Watergate affair.

President Nixon's proposals seem to have pleased most people, but they have been criticized by some for failing to take just account of environmental concerns, and by many for failing to provide more money for energy research and development.

The energy message is the most comprehensive declaration so far of the Administration's plans to deal with what has become popularly known as the great energy crisis in the United States, but which President Nixon prefers to call an "energy challenge". The basis of the energy challenge, problem or crisis is by now well known. Stated simply by Mr Nixon last week, it boils down to the fact that US "energy demands have grown so rapidly that they now outstrip our (US) available supplies, and at the present rate of growth, (US) energy needs a dozen years from now will be nearly double what they were in 1970". With 6 per cent of the world's population, the United States consumes about a third of the energy used in the world.

The upshot of the difference between domestic supply and demand is that the United States has found itself importing large amounts of fossil fuels, chiefly oil from the Arab states. In 1967, the United States ceased to be self-sufficient in oil, by 1972 it was already importing nearly 30 per cent of its total supply, and by 1985, it is estimated that import of oil will account for between 50 and 60 per cent of supply, 30 or 40 per cent of which will come from the Middle East. According to an estimate given last November by Peter G. Peterson, then Secretary of Commerce, by 1980 the US trade deficit in energy will amount to between $15,000 and $21,000 million a year.

In view of such figures, it is small wonder that many people have been crying "crisis". But energy shortages really hit home last Winter when supplies of fuel oil dried up in the Midwestern states, and for many others the energy crisis will become a reality later this year when some filling stations run out of gasoline. Such short term disruptions of supply are, however, a slightly different problem from the overall energy supply and demand situation.

Briefly, what happened last Winter stems partly from a shortage of natural gas, which started a couple of years ago. As deliveries began to dry up, many electricity suppliers switched to oil, precipitating a shortage there and refineries churned out fuel oil as fast as they could and produced less gasoline. The effects of that will be seen later this year. And then there have also been problems of siting refineries and lack of capital for investment in the oil industry.

At present, the energy picture is dominated in the United States by the three fossil fuels—oil, natural gas and coal—and each has its own special problems. Oil now supplies about 46 per cent of energy consumed in the United States, but demand is hopelessly outstripping domestic supply. Natural gas has about 32 per cent of the energy market, but its wellhead price has been pegged at an unrealistically low rate by the federal government and this has caused demand to soar while at the same time it has not been profitable for gas companies to prospect for new supplies and proven reserves have dwindled. The result: shortages have developed and pipeline companies have curtailed some supplies. Finally, the United States has about half the world's coal reserves, but persistent environmental problems associated with strip mining and with air pollution have been partly responsible for the fact that coal's share of the energy market has dropped from more than half immediately after the war to about 17 per cent today.

This is what President Nixon last week proposed to do about the supply of the three chief fossil fuels. As far as oil is concerned, he proposed to increase

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Congress's Priorities

by our Washington Correspondent

CONGRESS has consistently voted in the past few years to give the National Science Foundation large increases in its budget for education and graduate student support programmes. But the White House has been equally consistent in refusing to spend the extra money. That particular pantomime will not occur again if the House subcommittee on Science, Research and Development gets its way, however, for the subcommittee last week passed a bill which, among other things, would severely restrict President Nixon's power to impound funds voted for the NSF.

The measure, which is tucked away in the annual authorizations bill for the National Science Foundation, would allow President Nixon to withhold funds from the NSF only if each of the foundation's programmes is reduced by the same proportion. In other words, if the measure survives the rest of the Congressional mill intact, the White House would no longer be able to withhold money from specific NSF programmes.

The full committee on Science and Astronautics will consider the subcommittee's proposal early in May, after the Easter recess, and is expected to pass it. But the prospects in the Senate are less certain. For one thing, the authorizations bill will be dealt with by Senator Kennedy's NSF subcommittee, and Kennedy may not be willing to agree with a measure which would still allow President Nixon to impound money without first having to get Congressional approval.

In the continuing battle between Congress and the White House over who has final control over the Federal government's pursestrings, the Senate has agreed on an approach, spearheaded by Senator Sam Ervin, which would force Nixon to get Congressional approval each time he impounds any money. Kennedy would thus probably want a stronger anti-impoundment measure than one which tacitly assumes that the President has the right to impound money, even though it places considerable restrictions on how the money could be impounded.

Kennedy's subcommittee will probably hold hearings on the NSF budget early in May. During hearings before John Davis's Science, Research and Development subcommittee earlier this year, Dr H. Guyford Stever, director of the NSF, took exception to the anti-impoundment proposal because its inflexibility would prevent the foundation from altering its spending patterns as conditions change. But spokesmen from education associations welcomed the move.

short-term supply by scrapping a system of import quotas established in the 1950s. The result should be to increase imports of oil, particularly from the Middle East. For the slightly longer term, he urged Congress to clear away the legal barriers preventing construction of the Alaska pipeline and directed the Secretary of the Interior to step up the leasing of the Outer Continental Shelf for oil exploration and to allow leasing beyond the 200 metre isobath. It is estimated that the outer shelf holds about 186,000 million barrels of oil (about 45 years supply at the present rate of consumption) which is recoverable with existing technology. As for Natural Gas, President Nixon has proposed that Congress should amend the Natural Gas Act to deregulate the wellhead price of gas so that the price will increase and make exploration more profitable. Finally, he urged Congress to pass the Administration's bill to regulate strip mining so that uncertainties will be removed and coal companies can get on with stripping coal from the land, and hopefully clear up afterwards. He also suggested that states should ease their rules for meeting secondary air quality standards specified by the Clean Air Act, to enable coal with a relatively high sulphur content to be burned (the secondary standards are designed to preserve general welfare by preventing damage to plants and materials) and pointed out that his budget increases the amount of money devoted to removing sulphur dioxide from stack gases and sulphur from coal.

As far as nuclear energy is concerned, President Nixon announced no new policies, but reiterated the Administration's plans to give the liquid metal fast breeder reactor high priority in the energy supply picture. Nuclear energy at present provides only about 1 per cent of energy consumed in the United States, but is expected to increase its share to about 30 per cent by the year 2000.

So much for the supply side of the equation for the next few years, but what about the demand for energy? Energy consumption in the United States has been soaring since the war, but only recently has there been serious discussion of curbing demand. President Nixon's message last week had many pious words to say about the need for energy conservation, but his two chief proposals—that an Office of Energy Conservation should be established in the Department of Interior and that manufacturers of energy consuming appliances should voluntarily label their products with respect to their energy use—are unlikely to make a big dent in demand. A more direct but less politically appealing means of reducing demand would be to increase energy prices, but the proposals announced last

week, with the exception of deregulating natural gas, are more designed to ensure adequate supplies of cheap energy.

The loudest blast of criticism directed at the energy message has focused on the fact that it provides no new money for research and development for new sources of energy. Instead, President Nixon merely reiterated that his budget for the 1974 fiscal year increases expenditures on energy research to $772 million, up from $642 million this year. That amount is clearly unsatisfactory to many members of Congress, however, for Senator Henry Jackson recently introduced a bill cosponsored by nearly thirty colleagues, calling for expenditures of $2,000 million a year over ten years on non-nuclear research and development, and a task force in the House of Representatives has also called for an extra $1,000 million a year. In reply to his critics, however, Mr Nixon said "it is foolish and self-defeating to allocate funds more rapidly than they can effectively be spent".

Other criticisms have come from environmentalists, annoyed at Mr Nixon's suggestion that the states should go easy on implementing the Clean Air Act, and critical of plans to exploit offshore oil and gas reserves. Offshore oil wells have had a bad name ever since a blowout in a rig in the Santa Barbara Channel dumped a huge oil slick on the California coastline a few years ago. But Mr Nixon said in his message that "new techniques, new regulations and standards and new surveillance capabilities enable us to reduce and control environmental dangers substantially". He also announced that he has asked the National Academy of Sciences to study the environmental effects of possible oil production in the Atlantic Outer Continental Shelf and in the Gulf of Alaska. Environmentalist groups are also disappointed that the energy message did not increase funds for development of clean sources of energy such as solar power.

Finally, as far as organization of energy policy and programmes in the Federal government is concerned, the energy message announced that President Nixon will soon send to Congress a plan for reorganizing executive departments along functional lines. This will include the setting up of a Department of Energy and Natural Resources, which will take in energy programmes of existing agencies, including the civil power programmes of the Atomic Energy Commission. The focus for the new Department's responsibilities for energy will be in the present Department of Interior, for Mr Nixon said last week that he has directed the department to strengthen its organization of energy activities and its "capabilities for overseeing and coordinating a broader range of energy research and development".

A move to strip the civilian power programme from the AEC would, of course, turn the agency into little more than a weapons supplier for the Defense Department.

FOETAL RESEARCH

An Abrupt Ban

by our Washington Correspondent

The difficult ethical question of whether the Federal government should sanction research on live, aborted foetuses which have no chance of survival for longer than a few minutes, was abruptly settled last week. Dr Robert W. Berliner, Deputy Director of the National Institutes of Health for Science, told a crowd of Catholic high school students that he knows "of no circumstances at present or in the future, which would justify NIH support of research on live, aborted foetuses". The students had descended on the NIH campus in protest two days after the Washington Post disclosed that the ethics of such research are under discussion at NIH.

Although Berliner's statement was a personal one, he made clear that it was supported by other NIH officials, including Dr John Sherwood, Acting Director of NIH. And NIH spokesmen have since confirmed that no research will be carried out on live, aborted foetuses with NIH funds, at least until a committee which is examining a range of ethical issues involved in human experimentation has had a chance to report on the matter.

The committee, which has been meeting under the chairmanship of Dr Ronald Lamont-Havers, Deputy Director of the National Institute of Arthritis, Metabolism and Digestive Diseases, should produce its recommendations in two or three months' time. But Berliner's statement and the attitudes of top NIH officials seem to have prejudged official reaction to whatever the committee recommends.

Berliner also said at his meeting with the Catholic students that the NIH is at present funding no research on live foetuses and in fact little such research has been possible in the United States for two chief reasons. First, mid-term abortions are usually carried out in the United States by saline injection which damages the foetus so that it is dead when aborted. Intact foetuses, whose hearts are beating but which are too immature to live for more than a few minutes unless kept alive artificially, are usually the result of delivery by caesarean section. The second obstacle to such research was that until the Supreme Court recently removed all legal barriers to abortion within the first three months of pregnancy and allowed considerable discretion about mid-term abortions, many states outlawed abortion completely.

NEWS AND VIEWS

The Importance of Being Plume Conscious

IT is not difficult to identify thermal plumes in the mantle as the latest geophysical concept to be taken up in a big way ; and yet like any important, albeit essentially simple, idea whose time has come, it is not entirely new and without history. Rather more than the germ of the idea can be traced back at least a decade to Tuzo Wilson's (*Nature,* **197,** 536 ; 1963 ; and *Canad. J. Phys.,* **41,** 863 ; 1963) pioneering work on the space–time relationships of oceanic islands. In those days, of course, the seafloor spreading hypothesis itself was new, not yet having received support from the analysis of oceanic magnetic anomalies, and even continental drift was far from the near-universal acceptance it has today. Convincing evidence in favour of these phenomena was still being sought in the knowledge that exploration of the ocean floors was likely to play an important part ; but with access to the ocean floors limited, only oceanic islands offered usable data.

Tuzo Wilson's starting point was the realization that most truly oceanic islands were less than 100 million years old as represented by the ages of the oldest rocks then found upon them—a discovery which implied that such islands were either atypical of ocean floor regarded as old by geological tradition or representative of ocean floor necessarily young as a consequence of continental drift. The choice between these alternatives has long since been made on the basis of a wide variety of evidence including that from the oceanic islands themselves. What Tuzo Wilson did was to show that the distance of islands from the nearest oceanic ridge in the Atlantic and Indian Oceans increases generally with the age of the islands ; and this he took to be consistent with the view that ocean floor steadily moves away from the ridges. The explicit assumption here (supported by the presence of active or recently active volcanic islands such as Jan Mayen, Iceland, the Azores, Ascension, Tristan da Cunha and Bouvet along the Atlantic ridges) was that oceanic islands generally originate over the oceanic ridges but lose their activity as they move away from the source of magma represented by upwelling convection currents beneath the ridge axes.

But whereas this assumption seemed to be justified generally in the cases of the Atlantic and Indian Oceans, the oceanic islands of the Pacific told a different, or at least modified, story. Thus the simple age–distance pattern was not apparent in the Pacific ; and although it was possible to conceive of reasons for the absence of such a pattern which were still consistent with a ridge origin for oceanic islands, Tuzo Wilson chose instead to examine in some detail an alternative origin for Pacific islands, and thus suggest an important source of magmatic activity unrelated directly to either oceanic ridges or submarine faults.

The key to the problem was the way in which all active and recent volcanoes of the Pacific basin lying far from land and beyond island arcs apparently form linear chains trending west north-west to the west of the East Pacific Rise and east to the east of the Rise. Up to the early 1960s, these chains of islands and seamounts were widely interpreted as the results of lava extrusion from large faults in a rigid Earth. Although a progression of ages along each chain was recognized, the total age spread was not thought to be great and so it was just conceivable that the volcanic activity spread slowly as each fault gradually extended. Unfortunately, not only did the nature of the faulting prove impossible to determine but the range of ages along each chain turned out to be greater than previously supposed. Thus although each volcano in a chain had a similar history, the end members had reached quite different stages in that history separated by tens of millions of years.

Tuzo Wilson's solution to this dilemma was to suppose that the Pacific chains with their progression of ages were, as the Atlantic and Indian Ocean islands with their own age–distance pattern, manifestations of a spreading ocean floor, but with the difference that the source of activity was no longer necessarily an ocean ridge. Thus in terms of the convection current hypothesis, the magma source was seen as the relatively slow-moving interior of a convection cell whose surface was moving along above at a faster rate. Once a volcano formed on the ocean floor it would be gradually moved away from its initial position by the faster-moving part of the convection cell and become extinct, leaving virgin territory for a new, younger volcano to develop. The source of each volcano remains the same, and so each volcano has a similar history shifted only in time. Moreover, it is not necessary for the source to be immobile ; it need only move more slowly than the current above.

It is clear that Tuzo Wilson was, in effect, proposing the existence of what would now be called hotspots to explain islands of the Hawaiian type—surface manifestations of non-linear magmatic sources unrelated directly to the apparently more important linear sources represented by oceanic ridges. Moreover, there is a peculiar irony involved in that, in a particular sense, Tuzo Wilson's concept is closer to present day ideas than it might have been had it been proposed much more recently. To many, and perhaps most, geophysicists, the direct translation of Tuzo Wilson's proposals into present day terms would probably involve placing the magma source in the asthenosphere. This poses conceptual problems in that, on this basis, the source would be moving faster in the asthenospheric convection currents than the resulting volcanoes at the surface of the overlying lithosphere. Tuzo Wilson, however, was writing at a time when convection currents were regarded, if at all, as mantle wide. Thus his source could be placed deeper in the mantle, if necessary, and so, in retrospect, accord more closely with the origin of today's thermal plumes.

In the event, of course, the hotspot idea has been developed, most notably by Morgan (*Nature,* **230,** 42 ; 1971), in terms of magma sources largely independent of the asthenosphere in the direct sense, and in so doing has acquired several important characteristics apparently not

previously envisaged. For one thing, a worldwide system of hotspots is now envisaged as distinct from ridge activity, unifying conceptually sources of volcanic islands (and even continental volcanic centres) and aseismic ridges. Thus Iceland, situated on an oceanic ridge, is thought to be the result of a hotspot no less than the Hawaiian chain, which lies far from a ridge. Second, Morgan has proposed that hotspots are the surface manifestations of deep mantle plumes which bring up heat and "relatively primordial" material to replenish the asthenosphere, although it is not entirely clear yet whether this can be regarded as the sole source of the viscous asthenospheric material ultimately returned to the deeper mantle. But Morgan's most far-reaching suggestion is that plumes/hotspots provide the principal driving force for plate motions. Upwelling material along oceanic ridges and downwelling material along trenches, by contrast, represent near-passive processes contingent on the effects of the plumes. In other words, the primary manifestation of sub-lithospheric convection is the localized plume–hotspot rather than the large-scale cell mirroring the rise–trench system.

These are radical suggestions indeed ; and although it is more than two years since Morgan made them, it is doubtful whether many geophysicists have yet fully appreciated just how fundamental is the implied impact on concepts relating to the Earth's global behaviour. To be sure, there has recently been a flurry of activity in which thermal plumes and hotspots have been invoked to prove or disprove the existence of unrelated phenomena such as polar wandering ; but such studies have been hardly more than extensions in the use of Tuzo Wilson's original chain concept with the added assumption that hotspots are fixed relative to the mantle. The problem in assessing the validity of hotspots is, of course, that so little direct information about them is available. On page 565 of this issue of Nature, however, Schilling reports the results of a detailed geochemical investigation into the spatial and temporal characteristics of the supposed Iceland plume. In view of the potential significance of the plume concept, Schilling's important article deserves to be studied by all Earth scientists whatever their particular specialisms might be.   P. J. S.

Microarchaeology

ARCHAEOLOGICAL excavators are now experiencing advances in technique more radical than any since the 1920s and 1930s. Traditionally the role of the excavator has been to seek significant artefacts and the buried traces of former structures with which they are associated, enclosed and contained within the debris and earth of the archaeological site. Today, however, the recovery of such artefacts has become rather routine, and it is the information afforded by this debris and by the earth itself which is becoming a new focus of interest. A battery of techniques now being developed makes the processing of this material quite as informative as the study of the artefacts themselves. Equipment for flotation and sieving is taking its place beside the trowel and the spade in the indispensable armoury of the digger.

It is now some fifty years since Sir Mortimer Wheeler established definitively the principles of controlled stratigraphic excavation, admirably set out in his *Archaeology*

Works of Man

MORE than half a century ago, in 1921, the Swedish geologist Dr J. G. Andersson, noticed small fragments of white vein quartz among material that had fallen from an exposure of a fissure deposit into a quarry at Choukoutien in the region of Peking. The significance of the occurrence was immediately obvious to him: quartz was "exotic" at this locality. He turned to his companions and explained dramatically: "Here is primitive man, now all we have to do is to find him." (One of Andersson's companions on this occasion was Dr O. Zdansky, who discovered the first fossil human teeth at this site, which later became famous as the type locality of Peking Man, *Sinanthropus pekinensis,* now known as *Homo erectus pekinensis,* of Middle Pleistocene antiquity.)

It is not without interest that the milky white vein quartz which was worked by primitive man in the Omo Valley, Ethiopia, about 1.5 million years earlier in time than the material at Choukoutien (which is between 400,000 and 200,000 years old) is also "exotic". At Omo, as at East Rudolf in Kenya (the site of an even older culture, see Isaac, *Science,* **173,** 1129 ; 1971), man by good fortune has been found before or concurrently with his tools. Remains of hominids were recovered from the Omo Valley in the late 1960s, and now Merrick, and his colleagues, De Heinzelin, Haesaerts and Howell, record, on page 572 of this issue of *Nature,* their discoveries in 1971 and 1972 of artefacts *in situ* in the upper members of the Shungura Formation. Only the activity of man, 2.0 million years ago, as Merrick *et al.* point out, can feasibly account for the localized concentrations of the quartz tools in the fine clay sediments. Indeed the quartz would have had to be transported from sources several kilometres distant.

These artefacts from Omo are about 0.6 million years younger than the pebble tools and flakes uncovered in 1969 and 1970 *in situ* at East Rudolf. These two primitive cultures, and that found in Bed I, Olduvai Gorge (known as Oldowan), together with their associated hominids and fauna, now provide opportunities for a comparative study of early palaeolithic man and his habits in East Africa during a span of several hundreds of thousands of years.

From a Correspondent

from the Earth (Clarendon, Oxford, 1954) and more than thirty since Bersu demonstrated in Britain the techniques of area excavation (*Proc. Prehist. Soc.,* **7,** 30 ; 1940), where large expanses of the site are cleared, without intervening baulks, to reveal the entirety of whatever structures may be indicated by postholes or other scanty traces. In such excavations, and indeed since the work of Schliemann a century ago, it was normal to collect the animal bones unearthed, or any obvious accumulations of carbonized grain, and submit them for specialist study. Such materials did not, however, become a principal preoccupation until twenty years ago, when the objective of much

research became the understanding of the origins of farming. But even then special recovery methods were not normally used for such materials, nor was very serious thought given to the effect of such techniques as were used on the quality or nature of the resultant data.

Perhaps the first systematic attempt to develop, on a deeply stratified site, recovery methods appropriate to such materials came in 1963 in the excavations at the early farming site of Ali Kosh in south-western Iran. All the excavated material was screened through a sieve, and selected samples were subjected to a water flotation process to recover carbonized grain. The flotation method for archaeological materials was first reported in the United States (Struever, *Amer. Antiq.*, **33**, 353 ; 1965), and modified at Ali Kosh by Hans Helbaek. As the excavators of Ali Kosh aptly commented: "While most Near Eastern archaeologists have dug for buildings and incidentally recovered a few seeds in the process, we dug for seeds and incidentally recovered a few fragments of buildings in the process" (Hole, Flannery and Neely, *Prehistory and Human Ecology of the Deh Luran Plain*, University of Michigan, Ann Arbor, 1969, p. 4).

Systematic sieving of a column sample is likewise an American innovation: it has for some time been used routinely on the shell middens of the Californian Indians, which are little more than mounds of discarded food refuse (Meighan *et al.*, *Amer. Antiq.*, **24**, 1 ; 1958), but only recently has it been applied coherently and systematically to a wider range of sites. In particular, water sieving has proved a particularly rapid and efficient means of recovering material, and a number of "machines" which systematize and speed the processes of flotation and sieving of the soil have come into use in the past two or three years (French, *Anatol. Stud.*, **21**, 59 ; 1971). They have been used to good effect by Dr David French, Director of the British Institute of Archaeology at Ankara in the institute's rescue excavations in the Keban area of east-central Turkey, and on his important and very early neolithic site, Can Hasan III.

It is now becoming clear, however, that the real significance of these uses is not simply in the increased recovery of material, but principally in the increased reliability of the data so

obtained as a basis for the quantitative reconstruction of early diet or, in the case of small artefacts, for a quantitatively valid assessment of the cultural equipment at the site. Several contributions to *Papers in Economic Prehistory* (edited by Higgs, University Press, Cambridge, 1972) make this point with great force. Two in particular, by Payne, demonstrate the great vulnerability of archaeological data to sample bias. Already the circumstances of burial and of preservation cause serious distortion: Payne has now shown clearly the severe bias that is introduced by considering material recovered by hand during excavation — animal bones for instance. Systematic recovery by sieving radically alters not only the quantities recovered, but the proportions of one species to another, whose estimation is, of course, the object of the exercise. Dennell, in the same volume, in discussing the interpretation of plant remains, shows how the results obtained depend greatly on the type of deposit recovered, whether from floors or middens, and emphasizes that only carefully controlled recovery procedures will permit of any distinction between these. Few archaeologists in the future are likely to accept as reliable any assertion

about early diet that is not based, at least in part, on the results of controlled sievings, themselves carefully interpreted.

Column sampling, for long regarded as an inadequate means of archaeological recovery, is in consequence of such studies again being found useful. It is, of course, a well established procedure in pollen analysis, and has previously been used for this purpose on archaeological sites lying in peat (Clark and Godwin, *Antiquity*, **36**, 10 ; 1962). And archaeologists are now coming to realize that an understanding of the processes by which the site was formed, geomorphologically, can make a significant contribution. This is now seen to apply, not simply to the great depths of natural deposit which often cover palaeolithic sites and which have for long been studied by Quaternary geologists, but to the cultural levels themselves which were formed as the result of natural as well as human activities. The tell mounds of the Near East, for instance, have never been investigated geologically or geomorphologically, although they are very prominent features of the landscape. The problem of their formation has now been tackled by Davidson (*Archaeometry*, **15**, 143 ; 1973) in an article which will surely

Function of Nuclear RNP Particles

THE presence of ribohomopolymer regions in nuclear heterogenous high molecular weight RNA (HnRNA) and in cytoplasmic mRNA has been recognized for some time. Although it is known that the synthesis of ribohomopolymers is a post-transcriptional event, the precise timing and location of the process are uncertain. The function of these homopolymer regions is also unknown, although it has been suggested that they have a role in the processing of HnRNA to produce cytoplasmic mRNA. It is satisfying, then, to read the report of Niessing and Sekeris in next Wednesday's *Nature New Biology* (May 2) which describes two enzymatic activities and a ribohomopolymer synthetase activity in rat liver nuclear ribonucleoprotein (RNP) particles.

Niessing and Sekeris investigated these enzymatic activities *in vitro* using isolated 30S nuclear RNP particles. Optimal incorporation of ATP, CTP, GTP and UTP into homopolymers was achieved at 15 mM Mn^{2+}. ATP incorporation into poly (A) was also obtained at 5 mM Mn^{2+} and at 12 mM Mg^{2+}. These three enzymatic activities have

distinct pH optima. Examination of the reaction products by high voltage electrophoresis of alkaline hydrolysates indicates that the ribohomopolymers are not synthesized *de novo* but are formed by the successive addition of nucleotides to a pre-existing polynucleotide. Homopolymer formation is independent of DNA but addition of rat liver nuclear RNA stimulates the reaction three-fold. Treatment of RNP particles with RNase eliminates ribohomopolymer formation. Thus it is probable that the HnRNA contained in the RNP particles serves as a primer for synthesis of ribohomopolymers. Inhibitors of transcription have no effect on the enzymatic activities of the homopolymer.

Niessing and Sekeris have previously found in the protein moiety of RNP particles an enzyme which cleaves HnRNA. The discovery now in RNP particles of ribohomopolymer synthesizing enzymes which operate at a post-transcriptional stage independently of DNA points strongly to the role of RNP particles as the sites of cleavage and further processing of HnRNA to produce mRNA in its cytoplasmic form.

be the first of many geomorphological studies of archaeological sites. By systematic sampling of the 11-metre stratigraphic column at the neolithic settlement mound at Sitagroi in north Greece, a sequential series covering the 3,000 year duration of the site was obtained. Phosphate and particle size analyses were undertaken and these show that the build-up of material on the site resulted from the deposit of material transported there solely as the result of human activity. They also suggest that the occupation of the site was interrupted for long periods, which has a significant bearing on the archaeological interpretation. Indeed such investigations give a foretaste of the day, to which one must now look forward, when each of the different layers which the archaeologist records on stratigraphic profiles and sections will be interpreted for him in detail by the geomorphologist.

These different developments, with their emphasis on controlled techniques of recovery, herald, it would seem, a new phase of cooperation between the excavator and the specialists. It is no longer enough for the archaeologist to take a few samples and send them back to the laboratory for analysis: this may suffice for some purposes, such as radiocarbon determinations, but not in a coherent study of the site as a whole. Other techniques for the study of the environment are currently being developed (cf. Evans, *Land Snails in Archaeology*, Seminar Press, New York and London, 1973) and these, and investigations of diet, can only be effected by specialists on the spot. Archaeological excavation, at least at the micro-level, in the recovery of samples for systematic quantitative interpretation, has become too complex a business to leave to the archaeologist alone.

From our
Archaeology Correspondent

PLANT CELL WALLS

New Structural Model

from our Phytochemistry Correspondent

PLANT cells are encased in a rigid wall in which cellulose, hemicellulose, pectic polysaccharide, protein and lignin are the principal structural components. These walls are of fundamental importance because they are necessarily intimately involved in all aspects of the growth, development and morphogenesis of plant cells. Cell growth is not possible without wall growth and thus an understanding of cell wall structure is a vital prerequisite to a deeper understanding of the regulation of development. A significant contribution in this direction is to be found in the latest issue of *Plant Physiology* in the form of a series of three long but cogently argued articles by Albersheim of the University of Colorado and his colleagues Talmadge, Keegstra and Bauer (**51**, 158 ; 174 and 188 ; 1973). In this impressive *tour de force* the structure of the primary wall of suspension-cultured sycamore cells is described and a new and highly intriguing model is proposed. The work was made possible by the availability of purified hydrolytic enzymes and by improvements in the techniques of methylation analysis using combined gas chromatography–mass spectrometry.

The results show that the primary walls of sycamore are composed of 10 per cent arabinan, 2 per cent 3,6-linked arabinogalactan, 23 per cent cellulose, 9 per cent oligo-arabinosides attached to hydroxyproline, 8 per cent 4-linked galactan, 10 per cent hydroxyproline-rich protein, 16 per cent rhamnogalacturonan and 21 per cent xyloglucan. The structures of the peptic polysaccharides and the hemicelluloses were determined by methylation analysis and form the basis of the first two articles and the third report deals with enzymological experiments carried out to determine the nature of the linkages between the various macromolecular constituents. By the sequential use of endopolygalacturonase, endoglucanase and protease, evidence has been derived for covalent linkages between the pectic polysaccharides and both the xyloglucan

and the structural protein. Purified xyloglucan binds strongly to isolated cellulose, but by hydrogen bonding, not by covalent connexions.

Based on these observations a new model of the structure of the sycamore primary cell wall is proposed in which the cellulose elementary fibrils are connected to the matrix by hydrogen bonds between cellulose and xyloglucan. The latter, in its turn, is crosslinked by covalent bonds to the other constituents through the pectic polysaccharides which are themselves attached to the structural protein, probably by means of 3,6-linked arabinogalactan chains attached to the seryl residues of the protein. Furthermore, the hydroxyproline residues of the structural protein are thought to be glycosylated by arabinosyl tetrasaccharides.

The attraction of this new model is that it immediately lends itself to conjecture with regard to one of the chief unsolved problems of plant physiology —the mechanism of auxin action. It is generally agreed that growth stimulation by auxin involves the rapid weakening of the primary cell walls. This process must occur by the sliding of cellulose elementary fibrils past each other. This weakening and sliding may involve enzymatic breakage of the crosslinks in the walls, but, as the authors point out, the new model offers a more attractive alternative.

The only non-covalent link between the structural polymers of the wall is the hydrogen-bonded connexion between the xyloglucans and the cellulose, and if the xyloglucans and the cellulose could move relative to one another extension of the wall would result. The authors propose an ingenious non-enzymatic creep in which the xyloglucan

Symmetric Transcription of SV40 DNA

LAST year Aloni reported that during the replication of simian virus 40 (SV40) in permissive monkey cells at least part of the viral duplex DNA is transcribed symmetrically to yield RNA molecules that are complementary to each other. For two reasons this finding was most unexpected. First, in most other systems that have been investigated in detail transcription is apparently asymmetric and involves only one strand of duplex DNA. Second, the SV40 RNA molecules that can be isolated from cytoplasmic polysomes of infected cells are not self complementary and at first sight seem to be the products of asymmetric transcription. To reconcile symmetric transcription with the accumulation in the cytoplasm of asymmetric RNAs that are not self complementary, one must postulate that the complementary RNA chains produced by symmetric transcription are partially

and specifically degraded. In *Nature New Biology* next Wednesday (May 2) Aloni reports further experiments probing these events.

He has confirmed his original finding that late in the lytic cycle of SV40 in monkey cells newly made SV40 RNA is self complementary. He has also shown that this RNA contains poly (A) tracts which are almost certainly added after transcription, not least because SV40 DNA does not contain poly (dA) or poly (dT) tracts. Combining his own data with those of others, Aloni proposes that at least 60 per cent of the SV40 genome is transcribed symmetrically, that poly (A) is then added to the 3' end of the complementary RNA molecules, and finally that each RNA molecule is partially degraded from its 5' end to yield non-complementary viral messenger RNAs which have 3' poly (A) tracts.

moves "like an inchworm" along the cellulose fibre, requiring only the simultaneous breaking of about four adjacent hydrogen bonds. This concept is capable of explaining the action of auxin on the basis that auxin activates a hydrogen ion pump within the cell membrane increasing the H^+ content of the wall; the lowering of the pH should enhance the loosening of the hydrogen bonds and thus make the postulated creep process more active.

PROTEINS

Hunting the Helix

from our Molecular Biology Correspondent

W. H. AUDEN has described a professor as one who talks in other people's sleep, and such also seems by now to be the fate of that intrepid body of theoreticians still tirelessly labouring at the deduction of protein folding from amino acid sequences. The effusions in this field are abundant, usually very hard to understand, and at least on casual inspection pose little threat to the crystallographers. From time to time, however, most protein chemists will probably feel an obligation to grit their teeth and try to find out for themselves how matters stand. In regard to globular protein conformation, the proposition that all generalizations are untrue can fairly be said to hold, and thus far the best that has been achieved is some quantitative expression of the observations that met the eye when the first globular protein structure was determined. A number of recipes for the identification of the sequences that will assume the α-helical conformation have been devised, and the most searching statistical analysis—that of Robson and Pain—has had a very considerable degree of success.

Nagano (*J. Mol. Biol.*, **75**, 401 ; 1973) now descants on this theme with an analysis for the three most prevalent conformations, α-helices, β-structures, and the loop or β-bend. He has searched for correlations with combinations of different side chains taken pairwise at separations from zero up to six residues along the chain. Whereas simple rules of thumb, in particular Edmundson's helical wheel, predicate that it is the third or fourth residue along the chain that determines whether or not the α-helix will be favoured, Nagano finds that the most important correlation implicates the next nearest neighbour. For loops, on the other hand, long range interactions become more important. The predictions of α-helicity and of pleated sheet structure are nearly 90 per cent correct on a favourable definition of error, and that of loops, which is harder, 64 per cent on the same basis.

Wu and Kabat (*ibid.,* 13) advocate a different formula for predicting the positions of α-helices in a sequence; instead of taking the residues singly, or pairwise, or in a combination of both, they consider instead triplet sequences along the chain. They have collected data on the backbone dihedral angles, which define the local conformation, from a series of proteins of known sequence and structure, in which are to be found 1,561 of the 8,000 possible triplet sequences. The favoured combinations of the two variable dihedral angles fall into a few zones in the conformational map, and for a sequence of a protein of unknown structure it is, therefore, probably adequate to assign values to the pair of dihedral angles for each peptide bond within a margin of 15°, in accord with values for both of the dipeptide and the three tripeptide sequences of which it is part. Using horse heart cytochrome c as test sequence, Wu and Kabat report that they can adequately match the observed dihedral angles in this protein (which is very low in α-helix) for 56 of the 103 peptide bonds. The answer is wrong for 17, and somewhere in between for 29. In some of the former, the information on the relevant triplets is scanty,

and others were in the vicinity of the haem group, and therefore arguably perturbed by this intruder. There is a marked tendency towards overselection of values in the α-helix range, which may to some extent be rationalized, for instance, by the unusually high helicity of some of the proteins used in compiling the reference data. Wu and Kabat suggest that where one is concerned with a family of homologous proteins, such as especially the immunoglobulins, the existence of different sequences with presumably the same dihedral angles allows a much better prediction of local conformation, which will serve until, as they say, high-resolution X-ray data became available.

Meanwhile, Ponnuswamy, Warme and Scheraga (*Proc. US Nat. Acad. Sci.,* **70**, 830 ; 1973) have continued the attempt to predict chain conformation by working outwards from each residue to take into account interactions with progressively more remote side chains. With parts of lysozyme as models, they find that the agreement with the real structure improves as the length of the peptide encompassed in the calculation increases. That is to say, progressively more areas of the conformational map are excluded, and the dihedral angles

Antigen Specific Product of T Cells

T LYMPHOCYTES, those of thymic origin, are versatile in that they seem to be capable of both helping B lymphocytes (of bone marrow or bursal equivalent origin) to synthesize antibody and being cytotoxic effector cells. Many of the analyses of the mechanism of homograft or tumour immunity postulate a central role for T cells, but there arise problems from their postulated duality of action. It is known from *in vitro* experiments that T-cell cytotoxicity can be blocked by various factors, for example, antigen, antigen–antibody complexes and antibody. The first two of these are probably capable of blocking lymphocytes by binding to their antigen receptors; the last two can probably efface the target by binding to its antigens.

The production of antibody and of the antibody component of complexes may require a T-cell helper effect. Thus T cells can both kill cells and facilitate the production of some of the factors which can prevent T-cell killing. In next Wednesday's *Nature New Biology* (May 2) Röllinghoff *et al.* indicate that either during cooperation or the response to a malignant isograft, T cells synthesize a specific protein which may help eventually to devise a common mode of action for T cells in what at present seem to be two disparate functional attributes.

Röllinghoff *et al.* took thymocytes

from Balb/c mice and incubated them with Balb/c irradiated plasma-cell tumour cells for seven days. Dead cells were removed and the remaining cells (T cells as adjudged by their sensitivity to an anti-theta antiserum) were subjected to a procedure whereby their surface proteins were radioiodinated. Subsequently proteins released from the cell surface were collected in the supernatant and their binding capacity for the specific plasma-cell tumour was determined. It was found that an IgM type protein released from the activated T-cell surface had 5–20 times greater binding capacity for the plasma cell tumour against which it had been stimulated than for a comparable but different syngeneic plasma-cell tumour. No binding cell surface immunoglobulin was obtained from non-stimulated T cells.

Other workers have shown that 7S IgM molecules are produced by cooperating T cells, and the present finding, if it can be substantiated, seems to indicate that production of an antibody by T cells is part of their mode of response to both transplantation and particulate or soluble antigens. The experiments do not indicate, however, whether the immunoglobulin produced by the activated T cells contributes to their cytotoxicity, nor is there evidence presented that any cytotoxicity is generated against the plasma cell tumour.

corresponding to minimum computed energy are not necessarily the same for a bond in a dipeptide as for the same bond in the nonapeptide, for example. Ponnuswamy *et al.* assert that at a chain length of nine the conformation begins to home in on the true geometry, so that long-range interactions between remote parts of the chain need often not be considered. The results, however, show that there is still a long way to go. The unpalatable fact remains that the experimental conformation of excised peptide segments is all but unrelated to their state in the native protein, so that failure to take account of long-range interactions is by no means a trivial limitation.

Crawford, Lipscomb and Schellman (*ibid.*, 538) have concentrated on the hairpin turn of the polypeptide chain as a structural landmark suitable for purposes of prediction. This turn is defined by four residues, and Crawford *et al.* convey the surprising information that no less than 33 per cent of the residues of the globular proteins in their sample are engaged in such formations, as against 34 per cent in helices and 17 per cent in pleated sheets. Asparagine, glycine and proline have a strong tendency to appear in the reverse turns. They are most often in the first, second and third position respectively, and tryptophan is frequently found in the fourth. A case for a special function for leucine residues is made by Chou and Fasman (*J. Mol. Biol.*, **74**, 263 ; 1973), who give experimental evidence that this residue confers the greatest stability on polypeptide α-helices. Its occurrence is most frequent in internal helices in globular proteins, and around the walls of crevices containing prosthetic groups, and Chou and Fasman suggest that it may have an important structure nucleation function.

On the nucleation of chain folding, Wetlaufer (*Proc. US Nat. Acad. Sci.*, **70**, 697 ; 1973) has found on examining the structures of many globular proteins that spatially separate compact folded regions are often present, by criteria which he defines, and he gives arguments why it might be anticipated that chain folding would ensue after the formation of independent conformational nuclei in each separate domain.

Some potential energy calculations on β-pleated sheets have been done by Chothia (*J. Mol. Biol.*, **75**, 295 ; 1973), who finds that a right-handed twist in the direction of the polypeptide chain, which corresponds to dihedral angles within one zone of the conformational map, makes for minimization of energy. This sense of twist turns out to prevail in β-structures in known globular proteins. A structure with a left-handed twist would have appreciably greater conformational freedom, with relatively large variability of dihedral angles.

PALAEOMAGNETISM

Dating Hadrian's Wall

from our Geomagnetism Correspondent

THE success of palaeomagnetism rests on the fortunate fact that many rocks contain magnetic grains which have very high coercive forces. When a rock forms, its magnetic components acquire a magnetization in the direction of the ambient geomagnetic field; and because many of the grains have high coercive forces, the magnetization becomes "locked in" to the rock, usually at temperatures between 500° and 700° C, and is thereafter largely unsusceptible to the vicissitudes of subsequent history. Accordingly, many rocks still contain a valid record of the direction of the geomagnetic field at the time of their formation, perhaps thousands of millions of years ago. The palaeomagnetist simply has to measure such directions to determine the properties of the Earth's magnetic field in the past.

Unfortunately, this task is frequently complicated by the fact that all grains do not have high coercive forces. The magnetic particles in any given rock sample are likely to cover a range of compositions, sizes and physical structures — all factors which determine coercive force — and thus a range of coercive forces. Grains throughout the whole of this range will acquire magnetizations in the direction of the original field; but grains with lower coercive forces will be less inclined to maintain the direction throughout time in the face of random temperature fluctuations. Thus if the orientation of the rock with respect to the external field changes (for

example, because of continental drift or because of field reverses), the grains with lower coercive forces may, and often do, lose their original magnetization and acquire a new one in the new field direction. In short, they are magnetically unstable and thus subject to viscous remagnetization which can take place in times ranging from seconds to hundreds of thousands of years.

To most palaeomagnetists, viscous magnetization is a nuisance to be removed (usually by thermal or alternating field demagnetization) before the more permanent record of the ancient magnetic field can be measured, although there have been numerous investigations of viscous magnetization as a phenomenon in its own right. Heller and Markert (*Geophys. J.*, **31**, 395 ; 1973) have, however, now attempted to put viscous magnetization to practical use in the dating of rock movements. The theoretical basis of their work is chiefly a series of investigations carried out by Néel (see, for example, *Phil. Mag. Suppl. Adv. Phys.*, **4**, 191 ; 1955) during the late 1940s and early 1950s. This theory is complicated, incomplete and probably defective in part, although with some modification and addition it has proved sufficient for the present purpose. Using the theory as a basis, Heller and Markert have developed a set of experimental procedures involving alternating field demagnetization to determine the time at which viscous magnetization began to form in any given rock.

The rocks chosen by Heller and Markert to test the method were quartz dolerites built into Hadrian's Wall near Greenhead in Northumberland, and they almost certainly originated from

Singularities and the C Field

ABOUT ten years ago Hoyle and Narlikar developed and published a model of the creation of matter which depends on a small and elegant modification of the field equations of general relativity. The modification was called the "C" field, a negative energy field whose gradient is not a conserved flux but has sources where matter is created. The motivation for this work was the steady-state cosmology according to which, in spite of the expansion of the Universe, the density of matter remains everywhere constant in time.

It is a measure of the rate of progress of observational cosmology that the original motivation for this work has largely disappeared; there are few cosmologists who now take seriously the model of the Universe which looks the same in every direction in every place at every time. But the need to modify the equations of general relativity remains, because the usual equations possess no solutions free from singulari-

ties. There is not even a model of a massive object collapsing under its own weight without an elastic repulsion. Penrose and Hawking and others have shown that singularities occur under quite wide and physically reasonable conditions. Several workers are seeking a quantization of the equations to avoid the singularity.

In next Monday's *Nature Physical Science* (April 30) Narlikar now points out that the classical modification made for the steady-state theory can also avoid the singularity. He presents the equations in a new way and works out two special cases. One is the steady-state theory with a constant matter density. The other is the big-bang model modified by the fact that the creation of matter at the origin is at the expense of the negative energy C field. The resulting geometrical structure is similar to that of a model with torsion put forward by Trautman (*Nature Physical Science*, **242**, 7 ; 1973).

the Upper Carboniferous to Lower Permian intrusions of the Great Whin Sill on the crest of which part of the wall was constructed. This is an ideal circumstance, for it is clear that all the dolerites were originally magnetized in the same direction because they came from the same body. Now, however, they are oriented randomly with respect to that direction and have presumably maintained their present positions since Roman times. Whatever viscous components the rocks may have had before removal by the Romans, the present viscous magnetizations must date from the construction of the wall. The Heller-Markert techniques thus effectively give an independent method of dating the building of Hadrian's Wall. An added bonus is that similar techniques may also be applied to the Great Whin Sill itself, the source of the dolerite in the wall.

According to Birley (*Hadrian's Wall*, Ministry of Public Building and Works, London, 1963), Hadrian's Wall was constructed during the first four centuries AD. According to Heller and Markert, the ages of the viscous magnetizations in three of the wall dolerites are 1,600, 1,800 and 2,400 years, respectively (average 1,933 years). The agreement is thus quite good, although the spread of measured ages indicates that the experimental techniques are subject to errors. It is perhaps unfortunate that the age of the viscous magnetization is apparently an exponential function of the parameters which are measured experimentally, so that any experimental error is magnified in the final result. For example, an experimental error of only 5 per cent will lead to error limits of 600 years and 3,600 years for the dolerite "dated" at 1,800 years. For this reason, and because of uncertainties in the basic theory, the agreement between palaeomagnetism and archaeology is really quite remarkable. But by the same token, if the Heller-Markert method is ever to be used widely, extremely high experimental accuracy will be required and statistical methods will have to be applied to large numbers of samples.

Finally, what of the Great Whin Sill itself? Because of the times involved in viscous remagnetization, it is evident that any viscous magnetization acquired in previous geomagnetic polarity epochs will have been completely erased by now. Thus as the Sill is older than the last major field reversal, its present viscous magnetization should date only from that reversal 700,000 years ago. The viscous magnetization age of the Sill obtained by Heller and Markert is 818,000 years. This is in fair agreement with the onset of the Brunhes epoch, although there must inevitably be some uncertainty in the effects of possible geomagnetic events occurring during the past 0.7 million years.

QSOs AND GALAXIES
Nature of Ton 256

by our Cosmology Correspondent

THE hypothesis that QSOs are, in general, associated with the nuclei of galaxies (see *Nature*, **242**, 18 ; 1973) receives a further boost in a recent issue of *Astrophysical Journal Letters* (**181**, L25 ; 1973). Silk and his colleagues report a detailed study of the nuclear and extranuclear regions of the peculiar object Ton 256. They conclude that the data are consistent with a two component model, where a central QSO-like object is embedded in a giant elliptical galaxy.

Ton 256 is relatively easy to study because of its small (by QSO standards) redshift of 0.131. Spectroscopically, it cannot be distinguished from a QSO but it has a fuzzy photographic image which covers as much as 9 arc s on 200-inch plates. Silk *et al.*, suspecting that "Ton 256 may be a prime example of an object intermediate between a quasar and (compact) galaxy", set out to determine the nature of the fuzz. They chose positions 2 arc s north and 4 arc s southwest of the object's nucleus, and compared the observed properties of the fuzz at those positions with those of the nucleus.

It seems that the fuzz is markedly different from the central object, showing no line emission even though the nucleus has hydrogen Balmer lines and OIII emission. The colours measured for the fuzz also differ from that of the nucleus and are similar to those of the outer portions of a giant elliptical galaxy.

Silk and his colleagues are able to unravel the probable properties of the two components of the system, assuming that the nucleus of Ton 256 contains a "normal" QSO, and these in no way suggest that the hypothesis is incorrect. The lack of emission lines in the light from the fuzz sets a limit on the amount of gas in the underlying galaxy, again well within the values plausible for a giant elliptical. There seems little doubt that the Ton 256 system is an almost classic example of the QSO embedded in a giant elliptical galaxy and as such will probably be widely referred to as an archetype if that model maintains the remarkable progress towards complete acceptance which it has made this year.

HIGH SPEED PHOTOGRAPHY
Versatile Technique

from a Correspondent

THE host for this year's spring conference of the Association for High Speed Photography, held on April 26 and 27, was the Physics and Chemistry of Solids (PCS) Section of the Cavendish Laboratory, University of Cambridge. The meeting was opened by Dr David Tabor, the present head of the PCS Laboratory, who briefly outlined how interest in high speed photography has developed in Cambridge.

Origin of Cosmic X-ray Background

THE enigma of the cosmic X-ray background seems close to being resolved, after ten years of observation. The sudden increase in the amount of data available, thanks to the success of satellite-borne X-ray instruments, has provided sufficiently stringent limits to make realistic theoretical work possible; previously, so few parameters could be tied down by observation that a wide variety of more or less complex models could be adjusted to fit the data. The flexibility of the situation is highlighted by the fate of the supposed break in the spectrum of this background at 40 keV. A short time ago it was one of the few features which all models had to explain; today, however, there is considerable doubt about whether the break exists at all and it seems that it may well be some kind of instrumental effect.

So where do theories of the X-ray background stand in the light of the latest observations? In next Monday's *Nature Physical Science* (April 30) Fabian relates the Uhuru data on extragalactic sources to the problem of the X-ray background. Radio sources, at least one quasar (3C 273) and clusters of galaxies are all now known sources of X-rays, and according to Fabian a summation of the contribution of these and as yet unidentified components can explain the background.

With a cutoff brightness for individual sources of 5×10^{-4} counts s^{-1}, a total of 3.4×10^7 sources is required; if the faintest sources are at 3,000 Mpc, corresponding to the Hubble radius, then the mean luminosity of the objects is 9×10^{42} erg s^{-1}. "The important factor," says Fabian, "is that the satellite data give a log N–log S plot agreeing both with the intensity and fluctuations as observed by rockets."

Locating the individual contributors to the background is, however, another problem. Many known sources of extragalactic X-rays have the wrong spectra to fit the bill and Fabian points out that the sought-for objects are probably relatively faint at other than X-ray frequencies. The answer seems to be to concentrate the search on those X-ray source error boxes which are relatively free from bright optical objects, for example those of 2U1443 + 43 and 2U0043 + 32.

In his introductory talk Dr J. E. Field (Cavendish Laboratory) described the laboratory's present high speed camera facilities, which include a 'Fastax', a 'Strobokin', three rotation mirror cameras, capable of microsecond framing rates, and two image converter cameras, the fastest being an 'Imacon' which can give up to twenty pictures at rates up to 10^7 frames a second. These cameras are being used to study many phenomena, including crack propagation, solid and liquid impact, laser irradiation of materials, and the initiation and growth of reaction in explosive materials. The fracture research covers both basic studies and topics of practical interest, such as cleaving of gem stones, the interruption of electric current by fast fracture and fragmentation processes in rock blasting.

Dr M. M. Chaudhri (Cavendish Laboratory) described how he has used high speed microphotography to investigate the detonation of explosives. He has successfully combined microsecond framing rates with magnification onto the film of approximately 10 times and has studied reaction fronts as they propagate through azide crystals, impact loading of explosives, processes occurring when a needle enters an explosive compact and electrical initiation.

Mr S. N. Heavens (Cavendish Laboratory) has used a continuous access rotating mirror camera (AWRE C4 camera) to study the behaviour of thin layers of solids and liquids when impacted in the drop weight test. This method, which involves dropping a weight, typically 5 kg, onto a thin layer, is used extensively for testing the sensitiveness of explosive materials. The advance here is that Mr Heavens has successfully photographed the event using transmission photography.

Dr J. J. Camus and Mr D. A. Gorham (Cavendish Laboratory) described their work on high speed liquid impact. Dr Camus has overcome synchronization problems with the Beckman and Whitley 189 camera by explosively driving a plate target against a suspended droplet. In some experiments the droplet has been formed into a two-dimensional disk of liquid, thus allowing the impact and flow processes to be studied in detail. An interesting result is that gases can be trapped between the impacting surfaces and that when these gas pockets subsequently collapse they cause pressure pulses. This is thought to be important in explaining the onset of damage in materials subjected to repeated low velocity liquid impact (as, for example, in steam turbine erosion). Mr Gorham has looked at the impact of high velocity jets (typically 700 m s^{-1}) on solids using an 'Imacon' camera which allowed him to trigger the camera from the event—a procedure which is impossible with a rotating mirror camera. He gave

several examples to show how high speed drop impact can damage laminate materials.

Three contributions from government laboratories were presented during the conference. Mr D. A. Barnsley (Royal Armament Research and Development Establishment, Fort Halstead, Sevenoaks) reviewed the high speed facilities available at RARDE and Mr J. F. Gilbert (Atomic Weapons Research Establishment, Foulness) and Mr B. G. Houghton (RARDE, Potton Island) described flash, radiographic facilities available in their respective laboratories. The two machines at AWRE, Foulness, are currently operable at up to 3 MV with a maximum stored energy of 60 kJ and an output pulse duration of 60 ns. With a target-to-film distance of 2.4 m reasonable exposure can be achieved after penetration of ~15 cm in steel. The machine at Potton Island operates at voltages up to 300 kV and gives pulses of duration 100 ns, which are capable of penetrating ~10 cm of steel.

Both Dr A. W. Palmer (City University) and Dr R. J. Dewhurst (University of Hull) have used 'Imacon' streak

photography—Dr Palmer to study the breakdown of dielectric liquids and Dr Dewhurst to study ultrashort light pulses from an Nd-glass laser: both events need picosecond time resolution. Dr Dewhurst has obtained a resolution of 9 ps using an 'Imacon' 600 with an S1 photocathode (an infrared tube).

Examples of the application of cinephotography were given by Mr A. R. Thompson (University of Sheffield) who has used a camera operating at 3,200 frames a second to study the burning in solid propellent rocket motors. The investigation has yielded valuable information about the factors which affect the stability of the burning. Dr N. Gane and Mr J. A. Williams (Cavendish Laboratory) have used a cinecamera at 32 frames a second to study the metal cutting process. In their experimental arrangement the work piece is moved under the tool in a controlled environment. The resulting film shows clearly how different the metal cutting process is under vacuum conditions, with the occurrence of marked adhesion to the tool and an increase in the thickness of the chip.

Origin of Archean Schist Relics

IN this week's *Nature Physical Science* (April 23), Litherland argues against certain existing and widely accepted models for the origin and evolution of the Archean basement, basing his case on the results of mapping Archean rocks in the Rhodesia Craton. The models in question are those which state or imply that Archean schist (greenstone) belts represent the sites of ancient volcano-sedimentary basins formed, and later deformed, by diapiric behaviour of the underlying primitive crust.

Litherland describes such models as non-uniformitarian in the sense that they take Archean shields to have been formed by the aggregation of separate diapiric granitic nuclei. His own (uniformitarian) conclusion, on the other hand, is that the so-called granitic nuclei are really the end result of a metasomatic process by which schist belts were left as relics of a "folded regional volcano-sedimentary succession in a 'sea' of various granitic rocks". It is for this reason that he refers to the four large schist bodies in the investigated northeast corner of Botswana (see map) as schist relics rather than schist belts.

As a result of his geological studies, Litherland concludes, specifically, that the area investigated was first overlain by a sequence of Archean sediments and volcanics, at which stage the supposedly underlying primitive crust was not visible. Following a deformation, which produced the present pattern of steeply dipping beds, there then occurred the emplacement of circular grano-

diorite intrusions and a widespread regional granitization resulting in large and small schist relics floating in tonalite/granodiorite. In other words, the schist relics are mega-xenoliths of the folded volcano-sedimentary succession rather than sites of isolated deposition, and the granodiorite intrusions represent an early phase in the granitic cycle rather than control of sedimentation and deformation by syntectonic diapirs. Subsequently, a second deformation occurred, imposing the dominant tectonic fabric on the area. Litherland's overriding point is thus that the whole suite of rocks can now be seen to have resulted from lateral accretion rather than from isolated deposition between "granitic nuclei" — a uniformitarian, rather than non-uniformitarian, process.
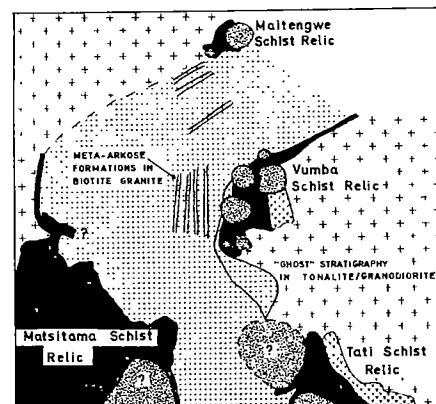
The suggested geological pattern in north-east Botswana before the second deformation, showing the four large schist relics.

Practical Application of Acupuncture Analgesia

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Acupuncture analgesia can sometimes be considered as an alternative to drugs, but it cannot be considered as a universal replacement. There are certain cases, however, where acupuncture analgesia is better than drugs and this technique needs to be developed further in order to assess its true significance. In this article two Chinese doctors, one of whom has conducted twenty-four operations using acupuncture analgesia, assess the advantages and disadvantages of using the technique in surgery.

SINCE the reported success of the use of acupuncture analgesia in several hundred thousand operations in China, great interest in this type of analgesia has been aroused all over the world. In Japan, America and other nations, medical people have begun to investigate the application of acupuncture analgesia in their daily medical and clinical work. This article is an attempt to give some explanation of the technique in order to assist others who are experimenting with it. It is based on the personal experience of one of us who has used this type of analgesia in twenty-four operations— three mitral stenoses, five lobectomies, six gastrectomies and ten thyroidectomies.

Acupuncture analgesia uses no anaesthetic drugs. Instead it is based on Chinese traditional medical theory, *Ching-lo,* which states that by applying pressure to certain specific points on the body, these points (on the meridians) will become numb. Pressure is applied by using a certain method of needling so that pain is either dulled or removed altogether. Thus, in using this technique during surgical operations, sensation in the area in which the operation is to be performed can be dulled while the patient remains entirely conscious.

At present in China this technique is widely used in both urban and rural hospitals and in mobile medical clinics. It has been used for surgery on the brain, neck, chest, abdomen and limbs. In addition, it has been applied in obstetric operations and in operations on the ears, nose and throat. Acupuncture has attained a definite place in Chinese medical practice and, when it can be used appropriately, has become the first choice of anaesthetic.

The use of acupuncture analgesia depends on the availability of properly trained manpower. A skilled medical team including anaesthetists is necessary. The team should be composed both of those who have expertise in the use of anaesthetic drugs and of those familiar with acupuncture analgesia. Those who have a thorough knowledge of both techniques are obviously the most valuable. Before the operation, one or two members of the team need to visit the patient to find out the patient's mental attitude, his desire to use this kind of analgesia and the nature of his illness. For their part, the team member or members should give a complete explanation of the anaesthesia technique to the patient.

In addition, the team of surgeons must be skilled, alert and capable. The doctors must be those whom the patient trusts, and they must have a thorough understanding of the patient's illness and mental attitude. Before the operation, they must give the patient a complete explanation of the surgical procedure and teach the patient to do the appropriate exercises such as deep breathing. The doctors must work quickly, steadily and accurately and must make the incisions and do suturing in the shortest possible time.

Particular Applications

To illustrate the use of this technique in surgery, we shall describe its application in a thyroidectomy, where the best results have been obtained. Two preliminary steps are necessary. First, the consent of the patient must be obtained. In addition to explaining the procedures to him, it is highly recommended that a demonstration be performed on the patient before his operation. Second, the individuals who administer the analgesia must have a thorough understanding of the procedures. We suggest that the anaesthetists practise acupuncture on their own bodies in order to discover the various methods of using the needle, the different sensations acupuncture produces and the proper depth to which the needle needs to be inserted.

About a half hour before surgery, 50 mg pethidine or other sedative is given to the patient by injection. The acupuncture needles are then inserted at two points on the hand and forearm. The first point is called the *hu ku* and is located between the thumb and the forefinger on each hand. The needle is inserted to a depth of 0.5 inch or until the patient begins to feel sensations of aching, heaviness, fullness and numbness. The other point is the *nei kuan* which is located posteriorly about 2 inches above the wrist. The needle is inserted to a depth of 0.5 to 1 inch, again until similar sensations are felt. If the needles are placed in the proper position and are rotated in a circular manner for about 20 min, an analgesic effect will be induced. The ensuing surgical procedure must be light and fast. When the skin is cut, the technique of "flying knife–rapid cutting" must be used as some pain may be caused when the incision is made.

Acupuncture analgesia does not completely remove pain. For this reason, electric cauterization must not be used to

stop bleeding. Instead, either ligation or pressure must be used. In addition, the patient must be warned that some uncomfortable feeling may be caused when the muscle is pulled around the neck and thyroid gland. The suturing procedure may also cause some pain and must be done as quickly as possible with sharp suture needles. If the level of pain increases, then the needles may be rotated again—or if that fails to bring relief, of course, drug anaesthesia may be resorted to. The whole operation should be performed very quickly to obtain the best results.

Advantages

There are many advantages to the use of acupuncture analgesia. Here we shall discuss three. First, as we have mentioned, acupuncture analgesia, unlike drug anaesthesia, dulls the nerves without causing the patient to lose consciousness; thus, it allows the patient and doctor to co-operate with each other. For example, again in a thyroidectomy, the doctor can talk with the patient at any time, and by listening to the patient's voice can discover if any injury has been caused to the recurrent laryngeal nerve. Another example is found in cases which involve heart and lung surgery. After the opening incision has been made the doctor can direct the patient to do deep abdominal breathing in order to prevent a sudden shift in the mediastinum and to keep the lung inflated so as not to interfere with the operation and ventilation of the patient.

Second, by comparison with the use of anaesthetic drugs, there are fewer physiological and psychological complications. During operations using acupuncture, we have observed that the blood pressure, pulse and breathing remain regular. This is often not the case with drugs. After an operation with acupuncture analgesia, there are no side effects nor evidence of the complications which may follow operations done with drug anaesthesia. Moreover, because there are few physiological reactions, the patient recovers his normal physical and mental state very quickly. In addition, the patient is more psychologically fit after an operation using acupuncture analgesia. According to our observations, the patient has been aware of and understood the entire surgical process as he has been conscious during the operation; therefore, when the operation is finished, he feels the surgery has gone smoothly and has been quite safe. He is very happy with the results. Often, he immediately wants to get off the operating table, walk around and eat.

Third, acupuncture analgesia is more convenient and comparatively cheaper than other known techniques.

Sometimes Inappropriate

One should not assume, however, that acupuncture analgesia is appropriate for all operations or a complete substitute for drug anaesthesia. Again according to our observations, the following factors impose limits on the use of this technique. First, acupuncture analgesia produces different results on different parts of the body. Our past experience has indicated that the results are better if the parts of the body involved are in the chest cavity and above. At present acupuncture analgesia is used in operations involving the head, neck and chest. As mentioned above, the best results have been achieved in thyroidectomies, so this type of surgery is being used for demonstration purposes. Other types of operation in which acupuncture analgesia has achieved good results are lung operations. In surgery on the abdomen and limbs, however, the results have been disappointing.

Second, the surgical cases must be selected carefully. When choosing a patient to undergo surgery with acupuncture analgesia, his illness must be considered. For example, in operations such as gastrectomies for gastric ulcers and pyloric stenosis, only if the operating time is short is it appropriate to use acupuncture analgesia. But for gastrectomies for stomach cancer in which a rather wide and long investigation is necessary, it is not wise to use acupuncture analgesia. For simple chest surgery such as localized pulmonary tuberculosis, acupuncture analgesia can be used. For exploratory surgery which takes time and in operations for widespread adhesions, it is, however, not advisable to use this technique. In conclusion, at the present time, cases should be chosen in which the nature of the disease is not too complicated and in which the operating time is 1 to 2 h.

Third, the emotional state of the patient must be considered. Because the success of the use of acupuncture analgesia depends on the willingness and understanding of the patient, this is a decisive factor. Before it is used, the entire procedure must be explained to the patient and his active cooperation must be enlisted. Thus, we select those who are emotionally stable, who have a high degree of confidence in the advantages of using acupuncture analgesia, and who are able to follow the doctor's requests and carry out his instructions. This kind of person is usually strong, energetic and young. Unsuitable types of patient include children under 10, who cannot cooperate with the doctor, and highly nervous individuals. In China, because thought preparation is thorough and deep, there are many people who have great faith in the doctors and nurses, and therefore many now volunteer for and even request acupuncture analgesia.

Problems

Acupuncture analgesia in clinical use is still in the initial stages of development. Our experience indicates that several problems have arisen in its application.

Acupuncture analgesia does not dull the nerves as completely and effectively as drugs. Thus, it is not suitable for every operation. On some occasions when the first incision is made, when suturing commences and/or when the procedure is long, the pain threshold may be decreased so as to render the analgesic effect relatively ineffective. It is therefore necessary to have drug anaesthesia available in case it must be used to complete the operative procedure.

Acupuncture analgesia does not cause complete relaxation of the muscles. For example, in abdominal surgery, during the operation the stomach and intestines might be disturbed which could result in a nervous reflex tightening the muscles and hence pain to the patient. If this condition does arise, drug anaesthesia may have to be used.

The theoretical investigation of the effects and uses of acupuncture analgesia is still in the early stages. The results of the use of this technique are only being brought to light through continued experience and experiments. Thus, at present, there is a method of systematic investigation to provide a firm basis for our work. We are now attempting to investigate the relationships between drugs and acupuncture analgesia. Although we believe acupuncture analgesia can be used widely, we feel it is misleading to say that it can and will replace the use of drug anaesthesia. At this stage we can only say that in certain cases acupuncture analgesia is better than drugs. Acupuncture analgesia is only a new anaesthetic technique, and in some contexts at least it may prove to be a better kind of anaesthetic skill. We believe that both acupuncture analgesia and drugs should be used in surgical work in order to further our understanding of the use of this new technique. We admit that it is a radical step to say it is possible merely to insert a needle, in the absence of drugs, to relieve pain. But at a time when the medical field is changing rapidly and new ideas are ever present, the importance of this development must not be neglected.

Features of a Closed-system Economy

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In a closed-system economy, gross national product is regarded as a "cost of the system". The Leontiev model relating the components of society's demand to resource use has been extended to make possible quantitative estimates of "social entropy" (dereliction, pollution and waste). This kind of work can be further developed, using general activity analysis and programming or optimization methods, to suggest a rationale for minimizing social entropy and real cost in a more advanced economy and technology. But much better thinking about values and objectives is needed for effective progress.

THE basic essentials of a rational economy, conservative environmentally and sensible thermodynamically, are contained in the important notion of "spaceship Earth" or a "closed system", suggested independently in 1966 by Kenneth Boulding of the Institute of ¡Behavioral Sciences of the University of Colorado, and by Barbara Ward (Jackson), now of Columbia University, New York City. Boulding has restated it several times but his approach is perhaps best illustrated in his essay[1] *Economics as an Ecological Science* in which he shows that, historically, the rate of creation of artefacts (knowledge, capital and technology) has outstripped even population expansion, making very high levels of the latter possible before an equilibrium is reached with the crossing of the artefacts and population curves, either by the artefacts becoming hostile to population increase (by pollution, war or exhaustion of resources, for example) or by such overcrowding that disorganization results in failure to innovate or create further wealth.

The choice may be, Boulding suggests, between the "Los Angelization" of the world by postponement of the artefact/population equilibrium point to very high levels, with massive overshoot and catastrophe, or a more gradual running down of resources (increase of entropy). His purpose in several contributions to this discussion is to speculate on the possible nature of a no-growth equilibrium society, to show in economic terms the parallel between our travelling celestial habitat and the situation of the astronauts and to demonstrate the need eventually, if not now, to operate economies and life-support systems with minimum rather than maximum effort and turnover.

As far as I am aware, neither Boulding nor Barbara Ward ever developed their concept, so the problem remains one of making what is now little more than a bright idea more articulate. This article is an attempt at a first step, to suggest further thought, study and criticism. The task, as so often, in developing new approaches is to present well known and familiar facts in a different light.

Closed System

The most important part of Boulding's idea is the recognition of gross national product (GNP) as essentially a cost of the system. In current "open system" economics, consumption and production are generally regarded as "goods in themselves" and GNP measures total throughput from "infinite" sources of exploitable materials to the infinite sinks (both outside the system) but is also viewed as a kind of index of prosperity. In a closed system, throughput is required to be a minimum and effectiveness is measured not by production and consumption as such, but by the "stock" of welfare including capital assets and overall quality of life support systems, including human capital, attainable with the least possible turnover. Any technology able to achieve its objective of improving the quality of life with minimal human effort and use of materials that is at minimum GNP (or, rather, gross national cost) would clearly be a good technology.

It is difficult to persuade economists, committed to "flow" ideas of welfare, to draw an analogy with the physical concept of entropy in the Second Law of Thermodynamics and equate real costs with the increases of entropy in a physical system, and yet a practical analogy with the Apollo systems suggests a closed-system terrestrial economics, merging "econosphere" and ecosystem, with an abatement technology based essentially on recycling and the redesign of products for reduced obsolescence and waste. Current open-system economics could in fact be charged with abstraction in excluding "sources" and "sinks" from its purview.

In *Economics as an Ecological Science*, Boulding is quite specific, and equates the gross consumption of society to real cost in the above sense, and so, according to him,

GNP = gross consumption (real cost) + excess
(used in improving the state of society)

The "excess" term he calls the welfare, state, or condition of society, which is broadly equated with its general capital structure—including human capital, for example education, welfare and life-support systems. Gross consumption includes all other items pertaining to a high level of activity, consumption and disposal. GNP is the gross cost of maintaining society, in terms of payments to the primary factors (the labour, land and capital of elementary economics), to be kept as low as practicable in a closed system, although the distinction between good (excess) and bad (consumption) costs is of course somewhat arbitrary. (The terms good and bad used here and later in this article, although inferred from Boulding's arguments, are not his descriptions but mine.) He suggests that misunderstanding of the real nature of GNP arises because highly developed societies tend to have a high throughput of energy, and energy use is correlated with real income per capita. There is also normally a high correlation between the throughput of production and consumption and the complexity and

elaborateness of society, but this should not lead one to think that the two (gross throughput and real wealth) are the same or that they need always be correlated[1].

Value-added (GNP) Cost of System

The difficulty of seeing GNP as a cost of the system arises, I believe, from the habit (possibly a consequence of accountancy conventions) of viewing it as the value added in economic activity, rather than as the cost of the elementary primary factors, which is the same thing. Yet it should be clear enough that the national income (or GNP, if external trade is omitted) is precisely the amount of the payments made in wages and salaries to labour and management, in profits for entrepreneurial services, in interest and dividends for the use of capital, and in rent, royalties and other sums for natural resources and land. Everyone would presumably agree too that an advanced technology able to provide real wealth with a minimum use of all these resources would be an excellent one, yet its use of primary factors, and therefore the value added, in the above sense, could be quite modest.

I have always found that clarity is helped by reference to the well-known model of an economy in equilibrium developed by Leontiev and his colleagues at Harvard. This model is so familiar to economists and statisticians that only the results required here will be indicated. (The model is described in all modern textbooks of quantitative economics. The treatment here is based on ref. 2.) Essentially it gives the components of the final demand, GNP or national income vector in terms of the gross outputs of industries or sectors of the economy, as well as key technical coefficients representing the input/output pattern of inter-industry flows or state of the technology. In the usual matrix form, it can be written as $Y = AX$ or in full.

$$
\begin{array}{ccc}
Y & A & X \\
\begin{pmatrix} y_1 \\ \vdots \\ y_i \\ \vdots \\ y_n \end{pmatrix} = & \begin{pmatrix} 1-a_{11} & & & \\ & 1-a_{ii}-a_{ij} & & \\ & & 1-a_{nn} & \end{pmatrix} & \begin{pmatrix} x_1 \\ \vdots \\ x_i \\ \vdots \\ x_n \end{pmatrix} \\
 v_1 & v_2 \quad v_j \quad v_n &
\end{array} \quad (1)
$$

The column vector Y represents GNP (or national income, omitting external trade); X is the vector of gross sector outputs; $A(a_{ij})$ is the Leontiev or technology matrix. The ith component of the GNP vector, y_i, is the scalar product of the ith row of the technology matrix and the column vector X, so that

$$
y_i = x_i - \sum_{j=1}^{n} a_{ij}x_j \quad (2)
$$

for all i. In other words, any component y_i of GNP is the gross output of sector i of the economy minus its sales or inputs to its own and all the other sectors or the amount going to consumer or final demand. Also, assuming linear relations, the general coefficient a_{ij} represents the input from industry i to industry j required to produce unit output of industry j, that is $x_{ij} = a_{ij}x_j$ where x_{ij} is the amount of the product of industry i consumed in producing j units of the product of industry j.

The value of the total production or output of each sector j of the economy, in money terms, is obtained by adding the inputs or purchases from all other industries (column j) to the value added, V_j, or cost of the primary factors, labour, natural resources, enterprise, used by sector j, that is

$$
x_j = \sum_{i} a_{ij}x_j + V_j \quad (3)
$$

The total supply by each sector i is the total (intermediate) demand by other industries (row i) plus the final demand by

consumers, y_i, so that

$$
x_i = \sum_{j} a_{ij}x_j + y_i \quad (4)
$$

and as, over the whole economy, total production equals total supply or $\sum_i x_i = \sum_j x_j$ we have $\sum_i y_i = \sum_j v_j$ (gross product or value added the same as cost of all payments to primary factors).

Now the general coefficient A_{ij} (equation (1)) of the inverse Leontiev or technology matrix gives the production required by sector i of the economy to meet one unit of demand by component j of the national income (ignoring imports) and the inverse matrix generally gives the pattern of sector gross outputs for any shape of GNP, national income, or "social policy" vector, that is

$$
x_i = \sum_{j=1}^{n} A_{ij}y_j \quad (5)
$$

for all i. It is also therefore possible to find the demand created by any component j of GNP on any primary resource simply by multiplying each element of the jth column of the inverse matrix (A_{ij}) by the labour, natural resources, or other factor coefficient f_{hi} for each productive sector x_i, so that the factor cost of the jth component of national income is $\sum_i f_{hi} A_{ij}$ and the total factor use or cost F_h for all components of the national income (omitting external trade) will be

$$
F_h = \sum_{j=1}^{n} \sum_{i=1}^{n} f_{hi}A_{ij}y_j \quad (6)
$$

F_h being evaluated in physical or money terms for any primary factor, such as labour or natural resources, for any pattern of final demand or social policy.

Parallel with Thermodynamics

I believe that from this point it should be practicable to suggest an approximate definition for the social entropy created by economic activity. But care is needed with the analogy as one does not (as Boulding says) have a measure of entropy as neat as that of thermodynamics. Here, however, I take it to include the pollution, including thermal pollution, and waste of industry as well as the whole of the pollution and the currently irrecoverable bric-a-brac of modern society as consumers. A rationale for minimizing social entropy is any framework for deciding how far to pursue recovery and abatement by new technology, although the non-economic or cultural implications of a highly developed closed system are more far reaching.

Allen V. Kneese of Resources for the Future Inc., Washington, has extended the Leontiev model by the addition of pollution generation and abatement activities as further rows and columns of the matrix (A. V. K. and Clifford. S. Russell, personal communication). Using his approach further columns, $n+1$, ... $n+m$, can be added to represent costly abatement activities such as industrial recycling for all the industrial pollution, spoil and waste under the heading of social entropy, as well as m rows to represent their generation, both by the n ordinary industry sectors and as by-products of the abatement technology itself. Thus expanding, say, the lth row $(n < l \leq n+m)$ of the enlarged matrix

$$
\begin{array}{l}
a_{l1}x_1 + a_{l2}x_2 + \text{---} + a_{ln}x_n + \text{----} + a_{ln+m}x_{n+m} - x_l = y_l \\
\\
a_{n+m,1} \qquad\qquad\qquad\qquad\qquad\qquad -x_{n+m} = y_{n+m}
\end{array} \quad (7)
$$

showing that any such residual (l) generated by each of the n ordinary industry sectors as well as the abatement technology, minus the amount (x_i) by which this item is abated, is the amount reaching final consumers or the environment; y_i is
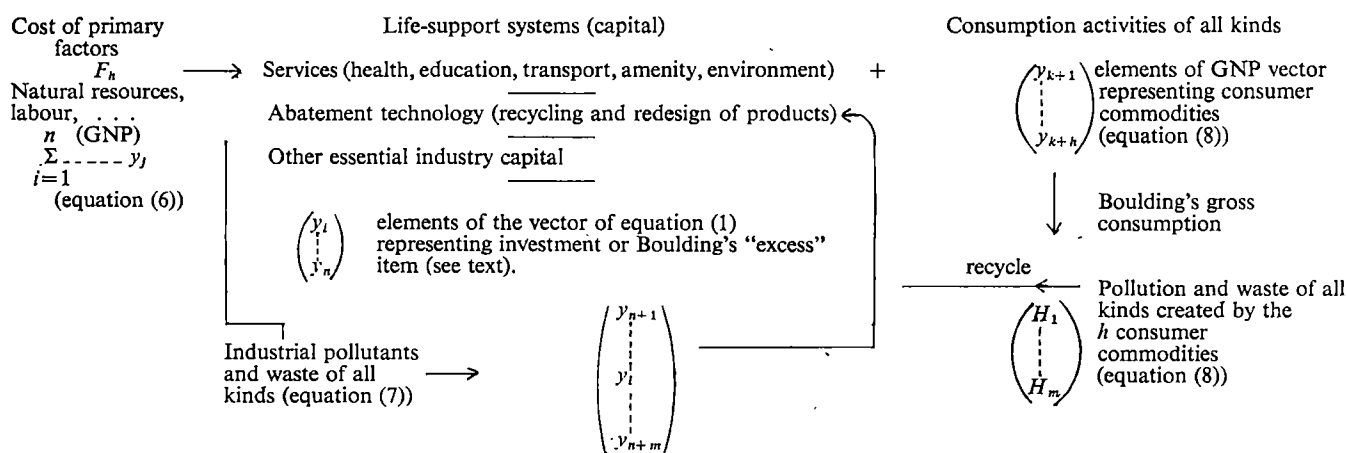
Fig. 1 Pictorial representation of equations (6), (7) and (8). It is not suggested that all consumption activities, which include, for example, food and other essentials and consumption for quality of life, are bad, merely that these are necessarily emphemeral and lead more rapidly to pollution, waste or social entropy. The excess costs represent more permanent structures or negative entropy (see text). Three interesting points arise from this discussion, in my view. (i) There is some current evidence of overcapitalization of industry (see ref. 3) in relation to the chemical industry, and there are undoubtedly other examples. If it can be shown, for example, by the application of equation (5) to a large region, that the gross output required to meet the bill of final demand is less than the technological limit of production, could it not be argued that the excess capacity served only to maintain a state of competition, but no environmental or social purpose? (ii) The MIT model[4,5] links capitalization directly to pollution, and reduction of resource use only leads to next limitation, a massive pollution crisis[6]. The reasoning of equations (7) and (8) is that capitalization only leads to pollution through the production of polluting industries. Future developments, such as the change from an industrial to a post-industrial or service society, and the effect of large-scale future investments in abatement technology, are likely to increase greatly the capital invested in life-support systems of society, as well, one hopes, reduce pollution and resource use below even current levels. The capital/pollution part of the MIT model therefore needs reformulating. (iii) The analogy of this arrangement of real costs with the Gibbs free energy equation representing the Second Law of Thermodynamics is clear enough.

here regarded as a component of the GNP vector Y (equation (1)), now represented by a column matrix with $n+m$ elements.

The social entropy created by society as consumers (or households, to use the economists' term) can also be represented, following Kneese, by a relation of the form

$$
\begin{pmatrix} H_1 \\ \vdots \\ \vdots \\ H_m \end{pmatrix} = \begin{pmatrix} --a_{ij}--a_{ih} \\ \\ a_{mh} \end{pmatrix} \begin{pmatrix} y_{k+1} \\ \vdots \\ y_j \\ \vdots \\ y_{k+h} \end{pmatrix} \quad (8)
$$

where the general coefficient a_{ij} is the amount of pollution or waste i, created for each unit of commodity j consumed $(k+1 \le j \le k+h)$. And the amount of each pollutant or waste H_i created by consumers is

$$
H_i = \sum_{j=1}^{h} a_{ij} y_{k+j}
$$

for all i. The h elements on the right side are the household consumer commodity components of the GNP vector Y (equation (1))*, and the total waste, or social entropy created by the production and consumption activities of society, will be the sum of the vectors †

$$
\begin{pmatrix} y_{n+1} \\ \vdots \\ y_i \\ \vdots \\ y_{n+m} \end{pmatrix} \quad \text{and} \quad \begin{pmatrix} H_1 \\ \vdots \\ \vdots \\ H_m \end{pmatrix}
$$

of equations (7) and (8).

* In other words $(k+1, \ldots, k+h)$ is a subset of the whole set (n) of all commodities going to final demand (consumers, government, exports and so on). It should be noted also that the coefficients of equations (7) and (8) can be found from industrial engineering and social survey data, an increasing amount of which is becoming available, although more is needed.

† I have here, for convenience, regarded the kinds of pollutants and other waste items $(n+1 \ldots n+m)$ as identical for industry and for society as consumers. This could be permissible if the range of significant items is chosen to include both, with zero coefficients in the matrices for industry or public as appropriate.

Fig. 1 is a simple pictorial representation of equations (6), (7) and (8), illustrating Boulding's division of GNP (paragraph 6) into the sum of two kinds of costs, namely good costs, applied to bettering the state of society, and the bad costs of simply pushing material through the system to maintain activity and employment—which need not, as he says, be correlated. The good costs amount really to negative entropy, creating highly organized and improbable structures of some permanence, and the bad ones, the rapid transformation of material by industry and general public into more probable and random states. There are no rewards or returns in the system, only the total costs of maintaining society, allocated either to improvement of the assets and infrastructure of a better life, or to consumption, much of it essential and valuable but nevertheless more directly related to running the system down.

Both kinds of cost are represented by equation (6) giving both gross product and its jth component in terms of use of resources (natural resources, labour and so on). The components $(y_{n+1}, \ldots, y_{n+m})$ of industrial pollution and waste, and of H (from consumers), also use resources. The distinction between good and bad costs could depend on the time factor and purpose, for example for the set $(k+1, \ldots, k+h)$ the disposal time is short, but clearly food and home-heating are essential. Nevertheless the wastage of modern society is extremely high and has a tendency to increase still further. On the other hand, investment, especially of the right kind (see Fig. 1), is potentially highly conservative and greatly beneficial to society. Investment in the life-support systems of society is included in the components $(y_1, \ldots, y_n)$ of national income, excluding the subset $(k+1, \ldots, k+h)$ representing immediate consumption. The value of the kinds of model described here is that they show the precise relationship between the components of society's demand and the gross outputs of sectors of the economy, including all significant wastes and pollution in terms of technical coefficients (in the matrix transformations) capable of being determined. The coefficients show which components of demand (y_j) make the heaviest call (through sector interdependence) either on polluting industries (equations (5) and (7)) or on especially valuable resources (equation (6)). Most important, they indicate (fairly precisely) the likely impact of detailed process or product redesign on the use of resources, and the possible

contribution of policies to discourage the consumption of commodities, especially in the subset $(k+1, \ldots, k+h)$. The Leontiev system does not, however, contain choice of technology within the model. By means of programming concepts one may be able to treat choice systematically to find the best policy for optimal results.

Rationale for Minimizing Social Entropy

Recent work by C. S. Russell and W. Spofford at Resources for the Future Inc. (A. V. Kneese and C. S. Russell, personal communication) has in fact moved from the simpler Leontiev input/output method in the direction of a full programming model, based on more general activity analysis, including industrial activities, recycling and the treatment, transport and disposal of residuals, as well as protective measures within a large region. This is essentially a flexible array of linked systems into which new ecological models (analytical or simulation) of diffusion processes, biological populations, and so on can be fitted as they are developed. Although the Russell–Spofford model is aimed at regional management problems in a conventional open-system economy, this kind of study could, in my view, lead to a more elegant mathematical description of a closed-system economy based on quite practical programming and optimization kinds of thinking. To me the most compelling current feature of the model is the construction of a general activity matrix $(m \times n)$ of m residuals (wastes and pollutants) and n activities $(n > m)$ including the activities referred to above. And, as the authors indicate, by-product production and recycling of materials to the input stream are conceptually similar and can be added to the activity columns of the matrix. We have in consequence a fairly major linear programming problem with constraint sets imposed by resource use and other factors. The objective function may, however, be non-linear, involving a series of controlled steps to an optimum solution, by iteration or hill-climbing techniques.

The method also provides at least a measure of our social entropy. In general the authors seek to relate a vector of residual discharges $(x_1, \ldots, x_m)$ to ambient concentrations of pollutants or wastes R at M locations in a region, in the form of a vector function $\mathbf{R} = Z(\mathbf{X})$, although the form of Z may not even be defined analytically and only discoverable by repeated runs of a simulation model to trace out an ecological response surface. Under very special assumptions (deterministic, steady state models with non-interacting residuals) the authors have suggested that their transfer functions could be constants, and it may be possible to write $\mathbf{R} = A(\mathbf{X})$ where A is a matrix of transfer coefficients, a_{ij}, relating the ambient concentration at region location i to a unit discharge of a residual from source j. The damage caused is not the social entropy itself but a measure of it, and if at a location i it is assumed to be a function of the ambient concentration of the kth residual, so that $DM_i = f(R_i^{(k)})$, the measure of social entropy in the whole region would be

$$D_E = \sum_{k=1}^{k} \sum_{i=1}^{m} DM_i^{(k)}$$

Differentiation of this equation with respect to each element of the residual discharge vector $\mathbf{X}$ gives the marginal damages or shadow prices for use in the objective function of the model. Although for simplicity the Russell–Spofford (RS) model considers the effects at M locations of residuals $(x_1, \ldots, x_m)$ from industrial sources, the social entropy created by the general public as consumers and the marginal costs could be included in the model by adding further activity columns to the general matrix to include the transport and disposal of such wastes to recycling centres and so on.

The (RS) model is concerned with minimizing cost in an open-system economy and the activity matrix, although containing a choice of technologies, does not include activities

to reduce the demand, F_h, on valuable resources by the feedback of residuals as inputs of production. Nevertheless, as the authors point out, the additional step would present no conceptual difficulties, and in my view this kind of modelling offers the best hope of practical progress in effective thinking about a closed-system economy. The redesign of products for durability or the recycling of materials could greatly increase the choice of satisfactory, conservative technological solutions lying within the feasible region of the programming model. Ultimately the range of technological possibilities and choices in a closed-system economy could be very wide, as recent work by the Institute of Technology of the University of Minnesota on the advanced systems modelling of an experimental city indicates *. The value of the RS kind of systematic modelling is also that it makes the cost and cost incidence of alternative schemes of management explicit and available to specialized management, regional government, or legislature. It also has a predictive element capable of suggesting the best rational first steps to more advanced, rational and conservative economies and technologies, at any rate on a regional scale.

Values in a Closed-system Economy

The technical argument of this article is that in economic and technological activity considered as a whole there is no profit or reward in an accounting sense, but only the costs of maintaining society (conveniently measured in money). These differ in kind, however, between those incurred in the creation of life-support systems, and educational and other services for quality of life in a post-industrial society, and those related to the throughput of energy and materials merely for high consumption and employment. The latter necessarily degrade the system whatever the time scale, so widely in dispute. I also suggest that a systems approach to economics could offer a wider choice of technologies to abate the demand on resources (F_h of equation (6)) and use them more rationally.

Abatement of the demand on resources means maintaining society and quality of life with less effort, or in plain language not doing everything the hard way. And although the theory of a closed system, merging econosphere and ecosystem, could evolve quite naturally, perhaps along the technical lines suggested by the Russell–Spofford model, the cultural implications of replacing social Darwinism with a systematic economics, nationally and internationally, are so profound that there seems some doubt of its feasibility, at any rate in this era, for it would need an effort of will and imagination from society of an entirely different creative order, of which there is little sign as yet.

Max Weber's well-known sociological study[9] *The Protestant Ethic and the Spirit of Capitalism* suggests perhaps better than any other how, historically, traditional economics has come to limit horizons and offer society but a single choice—to pay a man to do a job. This is not, of course, to denigrate the monumental contribution of J. M. Keynes to economic theory and practice. This was to show that the monetary system is not part of natural law, but subject to the control of governments, as well as to suggest the technical apparatus of control. But if a man can be paid to do a job which is not really required by society he can, with the same results, be paid not to do it; and Max Weber would have regarded the question as one for Calvinist philosophy rather than economics. Monetary policy has not been touched on here, but it seems probable that in a closed-system economy, Keynes's thinking would still provide a principal means of control. Investment in life-

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* The technology of an advanced urban complex is considered in the Minnesota Experimental City Project and related papers, kindly made available to me[7,8]. This study reviews means of power generation and storage, transportation, use and handling of materials, and design in a closed system. Although some of the technology is not now feasible, the emphasis is on the great potential (assuming some stability of demand), in terms of qualitative benefit as well as economy of resources, likely to be conferred by diversity and range of technological choice, together with logical systems of control attainable with the help of the modelling process.

support systems would probably be large, and multiplier effects considerable unless propensity to consume was reduced by removal of money from the system by taxation or other means. The alternatives of paying a man not to do a job (age of leisure), to do something else or, more generally, to increase the range of choice in life, are technically possible in a systematic economics, for the marginal productivity of labour and probably other resources is almost certainly already zero, and indeed negative for an increasing number of activities. But the objective of increasing the range of choice seems to this writer to be supreme, because it puts the essence of freedom (choice of life mode) before the form of it (political choice).

I have recently made some suggestions about the kind of approach one might hope for in a systems-oriented world[10], but it amounts essentially to putting objectives before organization and replacing the more directionless activities with time for reflexion about rational and human aims for society, as well as some agreement on which problems, scientific and social, are pre-eminently worth solving in this century. As regards the (at present) unquantifiable drop in demand for resources (effort and use of materials) potentially attainable by minimizing throughput, I would not be entirely averse to calling it, following the lead of another member of the meeting at the Royal Institution organized by *Nature* in April 1972, the "hedonistic factor"—although it is probably better to describe it more generally as the opportunity to increase greatly the range and depth of consciousness and awareness and to sharpen rather than dull the senses—in short to avoid one-dimensionality in man.

It is for this last reason too that I believe the authors of the recent *Blueprint*[11] may be mistaken as regards aims, because a rational modern society, however it may be constrained by circumstances, could hardly regard a Rousseau-esque existence in villages and forest clearings as an objective, or as anything other than one-dimensional and a system failure. I would hope for a post-industrial, but perhaps even more highly capitalized, society in a very special sense, with a number of key economic and environmental variables, possibly under automatic control—but, and most important, a more relaxed and appreciative age, aiming at style in thought and performance rather than mere intensity.

The paper on non-renewable resources, presented to the April 1972 meeting at the Royal Institution by Sir Kingsley Dunham, represented the current consumption curve for non-renewable resources as an isolated peak on the line of a very long time scale—a peak possibly to be characterized by our successors as a very curious interval during which the human race experienced a highly intensive but almost entirely one-dimensional life. The value of systems thinking and modelling is that it is a combination of the rational and the intuitive, in thinking about important problems in their entirety. Specialized education and professionalism carry the constant risk of fractional responses and poverty of imagination and approach.

It does not matter if the modelling of important problems is wrong and that the "scrappage rate" for models is high, for it is the process which matters. It is only important to break down disciplinary barriers, and to see that not only economists but scientists, ecologists, engineers and systems men should make a contribution in this area.

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Iceland Mantle Plume: Geochemical Study of Reykjanes Ridge

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Systematic rare earth and minor element concentration variations in basalt recently erupted along the post-glacial Reykjanes Ridge Axis and its northward extension over Iceland reflect the existence, spatial influence, and primordial nature of the Iceland hot mantle plume.

THE Reykjanes Ridge and Iceland (Fig. 1) are key features in North Atlantic and Arctic seafloor spreading[1-7]. It is also in the Iceland Region that the "hotspot" or "hot mantle plume" concept[8-11] has received support from geophysical evidence on the nature of anomalous mantle beneath the region[12-21].

In the Reykjanes Ridge–Iceland region it is possible to follow progressively fissure-type tholeiitic volcanic activity from beneath the sea up on land along the active Mid-Atlantic Ridge. Also, both shield building and fissural tholeiitic volcanism occur on Iceland and can be compared profitably.

Trace elements and Pb and Sr isotopic composition of "tholeiites" from oceanic islands are distinct from those of mid-ocean ridges[22-28]. These distinctions have been interpreted as reflecting different mantle sources and depth of origin for both types of volcanic activity. Hart[29] has stressed the difficulties of maintaining the distinct identity of the two mantle sources when both types of volcanism are closely related spatially and in an area of great mobility, such as for islands straddled on mid-ocean ridges (including Iceland).

Fig. 1 Dredge haul location along the Reykjanes Ridge Axis and neovolcanic zone extension over Iceland. ○, TR101; □, TR41; ■, fissure flow. Shaded strips are normal magnetic anomaly lineaments[4].
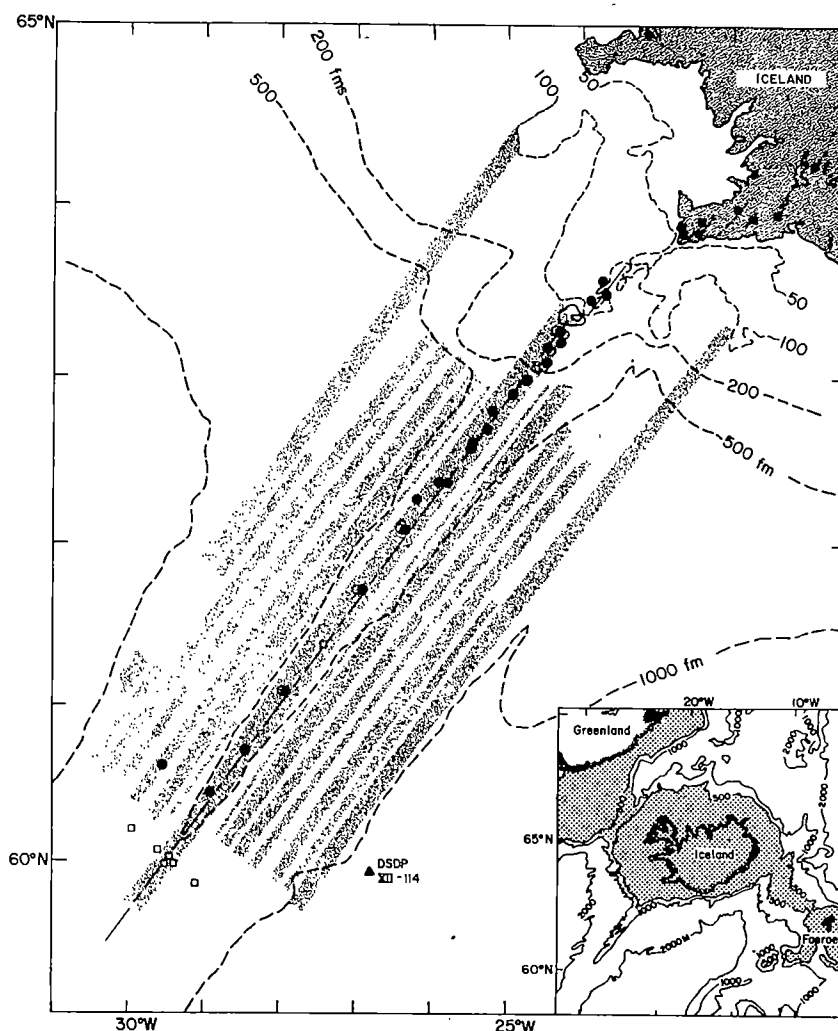
Taking the post glacial Reykjanes Ridge Axis and its extension over the middle neovolcanic zones on Iceland as a "geochemical window into the upper mantle", I now report results which not only infer the presence of a hot mantle plume rising beneath Iceland, but also reveal the extent of its present influence along the Reykjanes Ridge.

Post Glacial Geochemical Variations

During a cruise of RV Trident from July 17 to 19, 1971 (TR101), a nine-thousand-pound suite of fresh pillow basalts and crusts of post glacial age was dredged along the Reykjanes Ridge Axis (Fig. 1); the sampling was extended to historical basaltic flows erupted from known fissures along the middle neovolcanic zone of Iceland.

"Petrographically" the dredged lavas are typically submarine fine grained, vesicular and porphyritic basalts, with plagioclase, clinopyroxene and olivine phenocrysts occurring in variable proportions. The groundmass consists of the same minerals with some opaque minerals. Unlike many mid-ocean ridge tholeiites which are mostly devoid of clinopyroxene phenocrysts or xenocrysts[30-31], they are common in TR101 basalts. Modal abundance measurements show a progressive increase of pyroxene relative to plagioclase phenocrysts toward Iceland[33].

"Petrochemically" the basalts are classified as tholeiites according to the Yoder and Tilley normative scheme[32]. The analyses plot on either side but near the Di-En-Ab plane of silica saturation in the system Di-Fo-Ne-Qz. Most of the Reykjanes Ridge basalts are quartz-tholeiites, except four which are olivine-tholeiites. Four of the subaerial lavas overlap with the submarine lavas, and five others are olivine-tholeiites.

There is a noticeable tendency for the Fe content to increase relative to Mg towards Iceland, and similarly for Na relative to Ca. The $\Sigma FeO/MgO$ wt % ratio ranges from 1.2 at 60°N to 1.7 at 63°N, and is accompanied by an increase of the total iron from 10.5 to about 13 wt %. North of 63°N and on Iceland the scatter becomes larger. This is also true for other elements. The SiO_2 content remains remarkably constant along the ridge and its extension over the submerged Iceland Platform, ranging from 49.5 to 50 wt %. It drops markedly over the Reykjanes Peninsula and further north along the middle neovolcanic zone on Iceland (49-47.5 wt %).

"Geochemically," in marked contrast to petrological evidence (which in first order approximation indicates rather uniform tholeiitic basalts), the large incompatible trace elements such as K, La and the minor elements, Ti and P, show striking variations along the Ridge Axis up to Iceland (Fig. 2 and Table 1). These elements decrease regularly and progressively from Iceland where there is a larger scatter down to 61°N, and then level off until the limit of my survey is reached at 60°N. The progressive depletion is a regular function of the ionic radius for the rare earth series (RE). The smallest ion from Gd to Lu remains roughly constant while the light rare earths show more pronounced variations along the ridge axis. La, the largest rare earth ion, shows the greatest variation, and Sm an intermediate one. Thus La/Sm, or related functions such as ratio of enrichment factors relative to chondrites, confirm this point. The $[La/Sm]_{E.F.}$ ratio decreases markedly away from Iceland, possibly in a stepwise fashion (Fig. 3). This ratio is a good indicator of fractionation of the light rare earths and can, with the heavy rare earths, put rigorous limits on the genesis of these basalts[23]. Thus, the largest rare earths become increasingly depleted with distance from Iceland to increasingly resemble the so-called "low K_2O, light rare earth depleted submarine ridge tholeiites"[23,33,34]. At latitude 60°N the light rare earth depletion is more pronounced and the K_2O content lower than on any ridges.
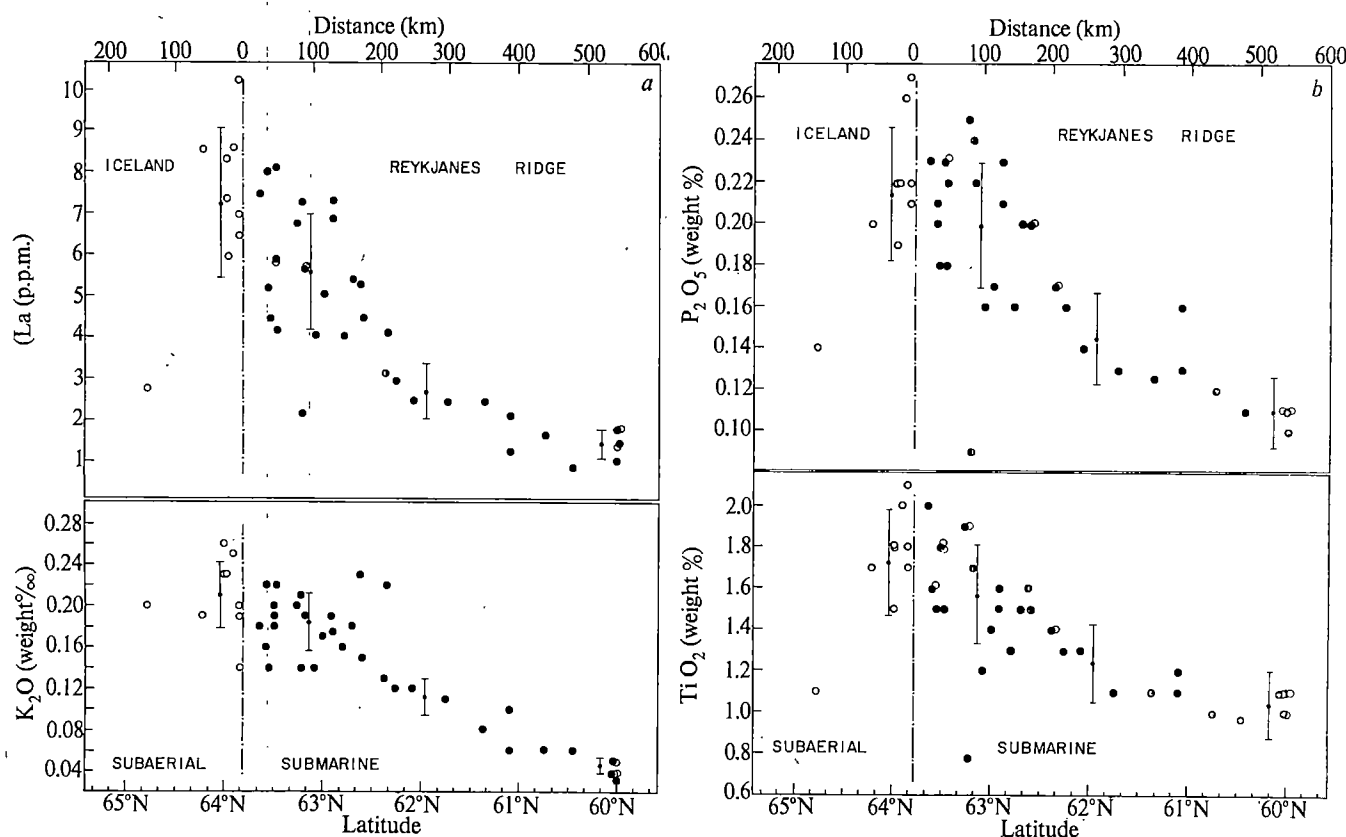
Fig. 2 La, K_2O, P_2O_5 and TiO_2 concentration variations in tholeiitic basalts of Fig. 1. The dispersion error bar was chosen equal to 15% for K_2O, TiO_2, P_2O_5 and 25% for La, to include analytical and sampling errors and possible post eruptional alterations. This excess scatter, or local noise, invariably increases as the submerged Iceland platform is approached. This corresponds to the region where the ridge is losing its morphological identity and magnetic anomalies II, III and IV become diffused or nonexistent[6].

The excess scatter over the dispersion error bar shown in Fig. 2 can be attributed to fractional crystallization at shallow depth. Ascents of magmas through a thicker crust[35] become more prolonged, intricate, complicate cooling paths at shallow depth, and enhance variations in fractionation.

What, then, does the geochemical trend represent? Could this mean that the light rare earth and potassium depletions of the world ridge tholeiites[23,36] are related to "hot mantle plume" activity, rather than the previously suggested early episodes of

mantle extraction of alkali basalts[37] or during continental growth[38]? Or could the chemical zoning simply represent a transitional zone of mixing between "hotspot" and mid-ocean ridge volcanic activity? Both possibilities recognize the existence of a hot mantle plume beneath Iceland.

Model Requirements

Any model describing the origin of the Iceland–Reykjanes Ridge System should allow for:

Fig. 3 Ratio of La over Sm enrichment factors relative to chondritic meteorites (Table 1) in tholeiitic basalts of Fig. 1. Dashed lines show possible groupings.
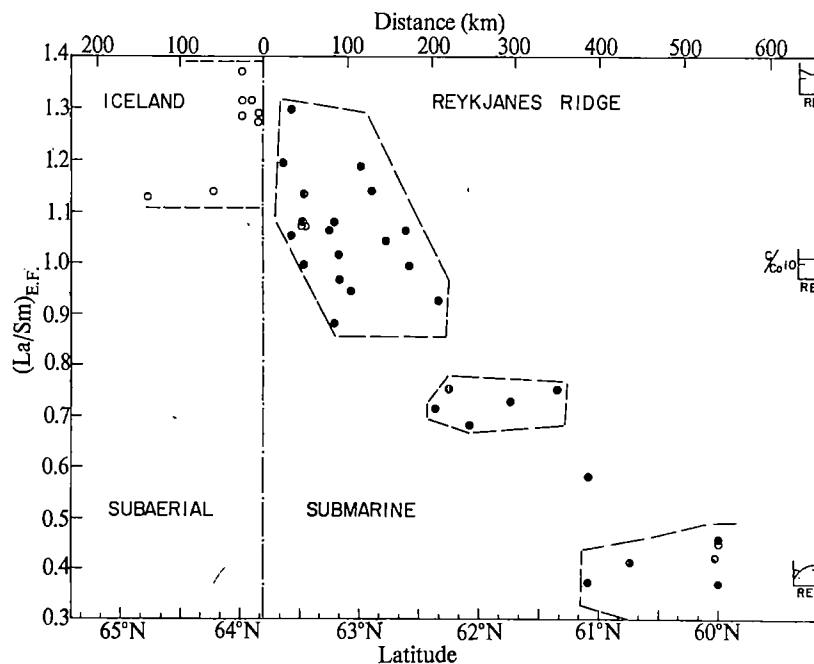
The Iceland bulge which is progressively decreasing in height and narrows along the Reykjanes Ridge—reflecting thermal expansion and/or upwelling of the mantle.

Geophysical evidence[12-15,39,40] suggests partial melting over a wider range of depth beneath Iceland than along the Mid Atlantic Ridge (MAR); from below the Moho to some 250 km.

Crustal thickness which varies from 8–16 km over Iceland[35] to 20 km along the Iceland Faeroe Ridge[41] and 3.5–4 km along and across the Reykjanes Ridge[4]. This suggests an unusually large production of magma along the Iceland rift relative to the MAR for the past 50-60 m.y., 2 to 4 times greater than across the Reykjanes Ridge as at 60°N.

V-shaped ridges symmetrically distributed about the ridge axis suggesting a component of mantle flow along the Reykjanes Ridge Axis[20].

Regular decrease of K_2O, TiO_2, P_2O_5 (and probably other large ionic lithophile trace elements) away from Iceland along the Reykjanes Ridge Axis.

Small but significant major element zoning.

Modal abundance increase of pyroxene/plagioclase phenocrysts along the Reykjanes Ridge toward Iceland.

The RE patterns progressively changing from slightly light RE enriched near Iceland to strongly depleted southward along the ridge, although the heavy RE stay constant[23].

The widespread and uniformly light RE depleted "tholeiitic ridge basalts"[23,33,34] dredged far away from any island (or hotspot) interferences as found on the Reykjanes Ridge around 60°N. This suggests a unique and uniform mantle source for these lavas of global extent taken to be the low velocity layer (LVL) in a partially molten state[23].

The low concentration of the large ionic lithophile (LIL) trace elements (K, Rb, Cs, Ba, U, Th, light RE) and radiogenic Pb and Sr isotopes[26,28] of these ridge basalts, which requires that this mantle source (LVL) be also depleted in these elements. The Sr and Pb isotopes further suggest that the LVL must have undergone such a depletion, by previous episode(s) of melting and magma extraction(s), at some considerably earlier time in the Earth's history[26,37,42].

The systematically higher concentration of LIL trace elements and radiogenic Sr and Pb isotopes observed in "oceanic island tholeiites", including Iceland and other proposed hotspots of tholeiitic composition. This suggests a localized source(s) in the mantle undepleted in these elements, which has remained as a closed system(s) for periods of time long enough to build up the higher concentrations of radiogenic isotopes.

The lack of secular RE pattern variations of tholeiitic basalts erupted at Reykjanes Ridge at 60°N and over the Iceland hot plume, but distinct for the two regions (my unpublished observations). This suggests that production of uniform primary

Table 1 Geochemistry of Reykjanes Ridge Samples

Station		Latitude	Longitude	Depth* (m)	La†	Sm†	Yb†	K_2O‡	TiO_2‡	P_2O_5‡	$[La/Sm]_{E.F}$
TR101	1D2	62°35.6'N	25°27.5'W	620-615	4.5	3.1	3.5	0.20	1.50	0.20	0.99
	2D1,2	62°37.4'N	25°26'W	650-615	5.3	3.5	3.2	0.23	1.60	0.20	1.07
	3D5	62°47.5'N	25°09.6'W	665-575	4.0	2.7	1.9	0.16	1.30	0.16	1.04
	5D2	62°54.4'N	24°53'W	555-455	6.9	3.9	3.0	0.20	1.50	0.21	1.25
	5D4	62°54.4'N	24°53'W	555-455	7.3	4.5	3.9	0.19	1.60	0.23	1.14
	6D9	62°59.7'N	24°41.9'W	450-350	5.0	2.9	2.2	0.17	1.40	0.17	1.19
	7D5	63°04.6'N	24°29.8'W	265-365	4.1	3.0	3.1	0.14	1.20	0.16	0.95
	11D2	63°16.3'N	24°12.4'W	50-100	6.7	4.4	3.2	0.20	1.90	0.25	1.06
	12D7	63°12.9'N	24°16'W	315-200	7.3	4.7	4.6	0.21	1.90	0.24	1.08
	12D40	63°12.9'N	24°16'W	315-200	2.2	1.7	1.9	0.14	0.78	0.09	0.88
	14D5	63°11.2'N	24°27.6'W	335-355	5.7	4.1	3.2	0.19	1.70	0.22	0.97
	15D5	63°34.7'N	23°42.2'W	100-65	5.2	3.4	1.9	0.16	1.60	0.21	1.05
	15D18	63°34.7'N	23°42.2'W	100-65	8.0	4.3	2.6	0.22	1.60	0.20	1.30
	16D4	63°27.9'N	23°52.4'W	65-55	4.2	2.9	2.5	0.22	1.50	0.18	1.00
	17D1	63°28.1'N	23°51.2'W	55-25	5.9	3.8	2.8	0.18	1.80	0.23	1.08
	18D1	63°28.1'N	23°51.2'W	46-40	5.8	3.7	2.8	0.19	1.80	0.22	1.08
	19D	63°28.2'N	23°48.2'W	140-70	8.1	5.0	4.6	0.20	1.80	0.23	1.14 .
	22D1	62°22.4'N	25°50.7'W	690-740	3.1	3.1	3.3	0.13	1.40	0.17	0.72
	23D1	62°21.3'N	25°46.8'W	675-640	4.1	3.1	2.7	0.22	1.40	0.17	0.93
	24D6	62°05'N	26°17.8'W	720-653	2.5	2.5	2.1	0.12	1.30	0,14	0.68
	27D11	61°44'N	26°52.9'W	605-595	2.5	2.4	3.0	0.11	1.10	0.13	0.73
	29D5	61°05.9'N	27°52.7'W	855-765	2.2	2.6	3.7	0.10	1.20	0.13	0.58
	30D10	61°05.9'N	27°54.2'W	825-760	1.3	2.4	2.3	0.06	1.10	0.16	0.38
	31D9	60°44'N	28°25.4'W	714-705	1.6	2.7	2.6	0.06	1.00	0.12	0.42
	33D6	60°27.4'N	28°53.1'W	950-895	0.85	2.0	2.1	0.06	0.97	0.11	0.30
	34D6	62°16.1'N	26°08.4'W	550-450	3.0	2.7	3.0	0.12	1.30	0.16	0.76
	35D3	62°42'N	25°12.3'W	650-510	5.4	3.4	3.4	0.18	1.50	0.20	1.11
TR41	18D2	59°59.7'N	29°32.5'W	940-1140	1.5	2.2	3.2	0.03	1.10	0.11	0.46
	19D	60°00.9'N	29°24.0'W	950	1.4	2.6	3.0	0.04	1.00	0.11	0.37
	20D3	60°01.2'N	29°20.8'W	860-1035	1.8	3.0	3.0	0.05	1.10	0.11	0.43
	22D1	60°01.2'N	29°28.5'W	930-1025	1.0	2.2	2.6	0.04	1.00	0.10	0.34
	38D2	59°59.1'N	29°31.5'W	890-960	1.8	2.8	3.7	0.05	1.10	0.11	0.45
	46D1	61°22'N	27°24'W	1625-1720	2.5	2.3	2.1	0.08	1.10	0.14	0.75
IC§	17	64°47.2'N	20°42.7'W	400	2.8	1.7	0.8	0.20	1.10	0.14	1.13
	36	64°12.6'N	21°01.2'W	250	8.5	4.5	3.1	0.19	1.70	0.20	1.14
	43	63°59.2'N	21°26'W	300	7.3	3.9	1.9	0.23	1.80	0.22	1.32
	47	63°58'N	21°44.5'W	460	8.3	4.2	2.3	0.26	1.80	0.22	1.37
	58	63°54.8'N	22°26'W	70	8.6	4.6	2.7	0.25	2.00	0.26	1.32
	62	63°58.7'N	21°58'W	140	5.9	3.2	2.2	0.23	1.50	0.19	1.29
HS§	524	63°51.25'N	22°41.8'W	10	6.4	3.5	2.0	0.14	1.70	0.21	1.27
	525	63°50.75'N	22°42.5'W	5	6.9	3.6	1.7	0.20	1.80	0.22	1.33
	529	63°51.8'N	22°26'W	80	10.2	5.5	1.4	0.19	2.10	0.27	1.29
Chondrites (Average of 20)					0.30	0.21	0.17				

* Depths for TR101 and TR41 are below sea-level, and for IC and HS are elevations above sea-level.
† Concentration in p.p.m., analysed by an instrumental neutron activation technique.
‡ Concentration in wt %, analysed by L. Shapiro.
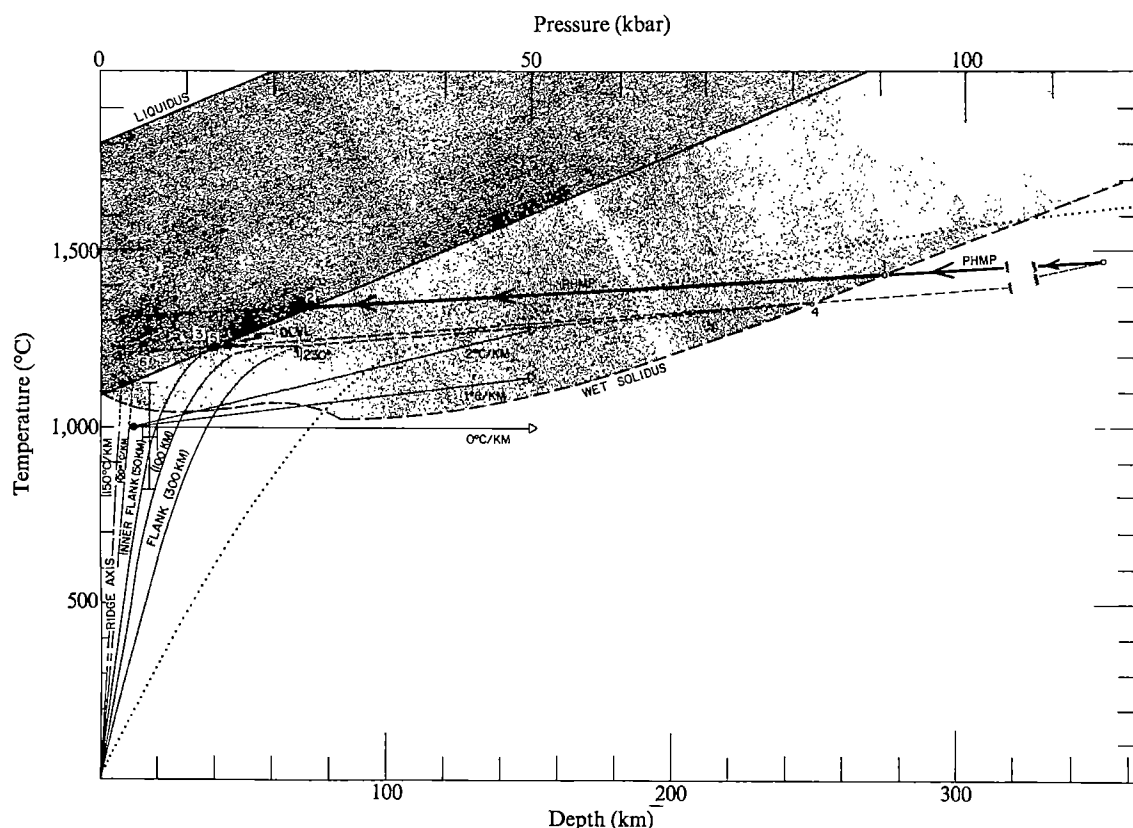§ Iceland samples.

Fig. 4 P, T, isoplethal projection[49,62] and path for both PHMP and DLVL during ridge injection. Beneath Iceland, 0-1 only PHMP solid rises, 1-2 incipient melting up to 5%, beyond 2 partial melting rapidly increases until the melt begins segregating around 3 or above[54,55]. Away from hotspot influence, DLVL path is difficult to ascertain because of uncertainties of prevailing geothermal gradients and actual lithosphere thickness. Using the Forsyth and Press thermal model[63], partial melting increases rapidly from 5 to 6 beyond which segregation becomes probable[54,55]. From latent heat due to decompression ($\Delta T \times C_p$) the maximum degree of melting[63,64] permissible $\gamma = \Delta T C_p / \Delta H_f$ is for PHMP 60%, and for DLVL 33%; more likely values are 20-40% and 10-15% respectively[54,62,66]. ΔH_f is the heat of fusion. Along transitional zone where mixing occurs, the PT path is indeterminate by this method[49]. Filled circle and error bars are upper mantle temperature and gradient range beneath Iceland inferred from magnetotelluric measurements[39,40].

magmas can be maintained for several tens of millions of years over two distinct mantle sources: one light RE depleted for the "low velocity layer", and the other light RE richer for the "hot mantle plume" source. Thus mantle-derived rare earth pattern variations in tholeiitic basalts seem to be functions relatively insensitive to time for certain periods, but rather sensitive functions of position relative to Iceland for the same periods.

The tectonic relations, chemistry, distribution pattern and relative volumes of rock types that are observed in Iceland[43-45]. This evidence suggests further magmatic and tectonic complexities beneath Iceland relative to the MAR, enhancing igneous differentiation and fractionation, and anomalous accumulations of melts by stagnation at shallow upper-mantle depths as well as within the Icelandic crust.

Single Mantle Source Models

With these requirements in mind I have explored several dynamical models, in which variation along the ridge of the mineralogy and chemistry of a single mantle source, depth of magma segregation, extent of partial melting and subsequent fractional crystallization during ascent and cooling of the magma occurs, as well as wall rock exchange and/or reaction. None of these single mantle source models can reasonably satisfy all the evidence at the same time.

For example, for lanthanum concentration (Fig. 2) to decrease with distance from the plume, the degree of partial melting would have to increase correspondingly, according to a simple trace element partitioning model I developed[37,46], and for any reasonable mantle mineralogy. This is the reverse of what would be expected from crustal thickness considerations[4,35], which requires 2 to 4 times greater extent of partial melting beneath the Reykjanes Peninsula. This, of course, assumes a direct relationship between volume of magmas erupted and degree of partial melting in the mantle beneath.

An alternative is to assume the magma beneath Iceland to be melt products of a smaller degree of melting but segregated over a larger volume of mantle (2 to 4 times as much). Melting would extend over a greater depth range and/or over a wider zone, in agreement with other suggestions[4,12]. But computer rare earth pattern modelling using variable mantle mineralogy and melting conditions indicates that the degree of melting would have to vary between 2 to 30% to satisfy the RE variation observed along the ridge. Production of quartz and olivine tholeiites over such partial melting range is untenable from an experimental petrology viewpoint[47], as is melting within a volume of mantle 15 times greater per unit ridge length beneath Iceland relative to 60°N.

A model assuming successive partial melting and removal of melts[37,46,48] along the Reykjanes Ridge Axis of a single primordial hot mantle plume flowing vertically beneath Iceland and sub-horizontally about the Iceland plume into the asthenosphere, also seems untenable, although it could be tailored to fit the rare earth pattern variations.

The model must be rejected on Pb and Sr radiogenic isotope evidence. $^{207}Pb/^{206}Pb$ is known to decrease southwestward along the Reykjanes Ridge up to 60° N (Sun, Tatsumoto and Schilling, unpublished); and similarly $^{87}Sr/^{86}Sr$ data available presently at 60°N are lower than on Iceland (Hart, Powell and Schilling, unpublished). This also eliminates the possibility of an increase toward Iceland of the extent of fractional crystallization during the ascent of lava derived from a single source, for explaining the general chemical gradients of Fig. 2.

Hot Mantle Plume Mixing Model

The model satisfying the requirements best is a mixing of melts derived from two mantle sources. These are the primordial hot mantle plume (PHMP) rising beneath Iceland, and

Fig. 5 Schematic flow patterns compatible with observed chemical gradients and mixing model[49]. Hatched zone represents influential depth range where upward diapiric injection can start. a, The density of PHMP and flow about the Iceland plume is rapidly used up by feeding the spreading axis. b, Showing the PHMP flow progressively sinking about the Iceland plume as a thunderhead[16-18], and the total plume discharged rate is larger than in a. c, The vertical PHMP flow rate is just sufficient to feed the growing lithosphere beneath Iceland, and its velocity pattern decreases to zero some 400 km away. The plume radius would have to be enormous (600 km) and this is very unlikely. Rheologically, cases a and b (finger-like flow configurations) may be difficult to realize and to be maintained. The problem may be alleviated considering that mixing may occur by complex flows of porous media into one another, percolation of melts and penetrative convection[58,67], because within the last 250 km depth, both PHMP and DLVL mantles are composed of partially molten rocks of slightly different density.
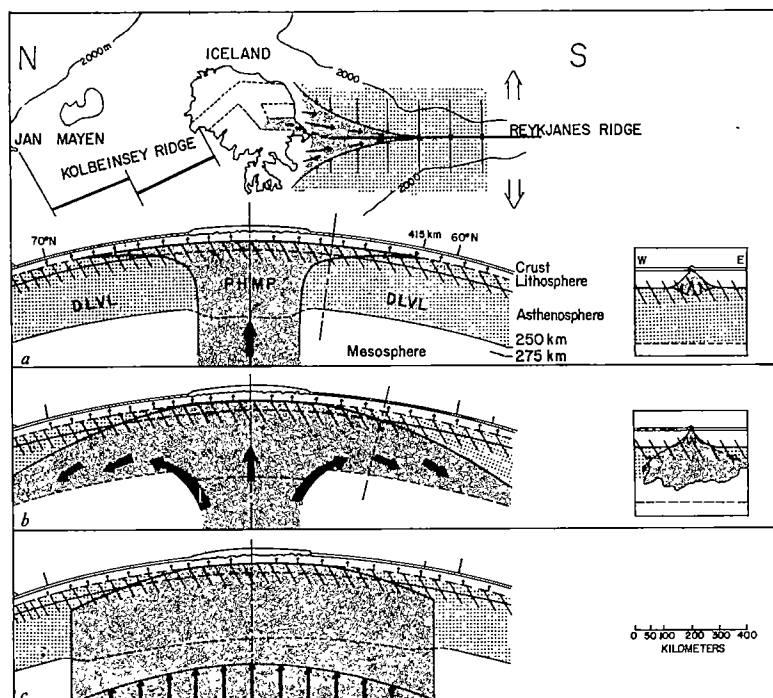
the more passive but more global low velocity layer depleted in large ionic lithophile elements and low in radiogenic Pb and Sr (DLVL). This latter source, usually away from any hotspot influence, feeds the spreading axis with accreting material for new lithosphere and crust generation. The PHMP flow rate is in excess of that required to create new lithosphere beneath Iceland, which is also spreading. During the rise partial melting begins, due to decompression melting[49] (Fig. 4). The overflow of PHMP is diverted into the low velocity layer (DLVL) either radially[16-18] (Fig. 5) or, more probably, by being preferentially channelled along the Reykjanes Ridge Axis, at the base of the lithosphere, where diapiric injection begins[20,21] (Fig. 5a). This zone is hotter, mass deficient, and structurally weak because of the spreading. The total Iceland mantle plume discharge is, however, not vigorous enough to feed the Reykjanes spreading axis along its entire length; material from the DLVL will complement laterally. A steady state becomes established. Along the zone of injection and over Iceland, either or both mantles rise, decompress, and partially melt; the two primary melts (and/or the two mantles) mix in proportions which vary along the ridge[49]. South of 60°N the new lithosphere and its upper basaltic crust is derived from the DLVL by passive lateral and upward flows in response to spreading[19]; and the melts are feldsparphyric low K tholeiites typical of mid-ocean ridges away from hotspot influences. Near Iceland lava is all derived from the PHMP, and the melts tend to be relatively richer in augite relative to plagioclase phenocrysts. In between is the zone of transition or mixing, where the PHMP contribution decreases regularly southward and the contribution from the DLVL increases.

Although petrologists have usually been reluctant to call for mixing of magmas to explain hybrid melts, their objections seem valid only when the end-member melts are of very different composition, such as rhyolitic and basaltic melts[50,51], or when mechanical conditions for mixing are unfavourable. The proposed mixing occurs between two types of basaltic melts of very similar bulk composition. Trace, minor and radioisotopes are indeed quite distinct, as their concentrations depend on the past history of their mantle sources and partial melting conditions, but the difference is insignificant in controlling immiscibility. Mixing of tholeiitic melts along the Kilauea Rift Zone has been convincingly demonstrated[52], and by analogy the concepts can be applied to the Reykjanes Ridge.

Two important mechanisms are available for the mixing of two component melts.

The first plausible mechanism is by mixing in elongated magma chambers lying beneath the ridge crest, mostly at the base of the crust[58]. The mechanical mixing occurs in part during segregation, coalescence of interstitial melts and during channelling when both mantle sources upwell and partial melting increases due to decompression (Fig. 4), but mostly in these elongated magma chambers. During diapiric intrusion of crystal-mush, the rate of magma segregation and upward movement is much faster than the residual solid once a threshold of degree of partial melting (ratio of liquid to solid) is reached[54,55]. Thus melts will tend to accumulate at the base of the crust, ready to feed the ridge axis which is intermittently spreading. There is circumstantial evidence in support of the proposed mechanism, such as the abundant presence of phenocrysts, and resorption and zoning phenomena. But I prefer to defer further discussion until a detailed electron probe study of TR101 collection is completed.

As an alternative hypothesis, the second mixing mechanism I believe plausible is horizontal dike propagation over long distances (>100 km) and parallel to the Reykjanes Ridge Crest volcanic edifice, in a similar fashion to that along the Kilauea Rift Zone[56]. Lava in Hawaii travels sub-horizontally more than 120 km, because of gravity induced symmetrical stress field present within elongated volcanic edifice.

Morphologically, the Reykjanes Ridge, featuring an elevated blocky or triangular central part[4], seems to be a reasonably close analogue of the Kilauea Rift Zone and its seaward submerged extension. Pillow basalts erupt on both[57]. Further, because of the ridge submergence down to 1 km of water along the transition zone, a horizontal pressure gradient of ~0.5 bar km⁻¹ ridge length should potentially be present along the ridge interior. Upon dike formation and tapping of elongated magma chambers at the base of the crust, there should be a tendency for PHMP derived lava to rise diagonally along the ridge with a significant southwestward horizontal component of velocity. Lava derived further away from Iceland, ultimately from the DLVL, will also rise diagonally, but less so, as the southwestward horizontal component of velocity decreases southwestward with submergence. Thus the path of both component melts cross, allowing mixing to occur in a similar way as described by Elder's experiments[58], and as petrologically documented by Wright and Fiske[52] for hybrid lavas erupting along the Kilauea Rift Zone in Hawaii. These two mechanisms need not be mutually exclusive, but may operate simultaneously, thus enhancing the chances of mixing.

Flow Patterns about Mantle Plumes

Although I have been able to ascertain the extent of the Iceland hot plume influence along the Reykjanes Ridge by using its axis as a window into the upper mantle, the geochemical approach does not allow me to distinguish between patterns of flow (Fig. 5), vertically or horizontally, nor between radial and pipe-like asthenospheric flows[16-18,20].

What can be ascertained is that the influence of the PHMP flow on the zone of magmatic injection must decrease progressively and die out some 400 km southwest from the tip of the Reykjanes Peninsula. This is more than 3 plume radii from the centre of the plume, assuming the plume to cover Iceland (radius = 200 km). Formulation of the mixing model and further references are given elsewhere[49].

Ridge Morphology

An intuitive approach to determine shallow asthenospheric flow is to consider the ridge morphology. Iceland and other hotspots represent significant bulges on the geoid, interpreted from gravity to reflect rising currents in the mantle[16,17]. The funnel shaped morphology of the Reykjanes Ridge suggests a forceful axial flow of PHMP from Iceland southwestward, perhaps with some piling east and west of Iceland. South of 60°N along the narrow part of the funnel ridge shape, only DLVL material feeds the ridge in response to spreading (Fig. 5). North of Iceland, the axial asthenospheric PHMP flow is probably more complex due to the proximity of the Greenland Continent which is underlined by a relatively cold upper mantle, and perhaps also influenced by the Kolbeinsey Fracture Zone. Thus a steady state flow pattern was more difficult to reach north of Iceland. This is reflected by more subdued morphology of the MAR, and several recorded jumps of the position of the active rift zone during the past 60 m.y. (ref. 59).

I suggest that the seafloor morphology over and around a hotspot region reflects the shallow asthenospheric flow of PHMP about the "thunderhead". A three directional starlike flow, more intense along the two MAR branches, would be predicted for the Azores hot plume, and similarly for the Afar hotspot[60].

It seems that at shallow asthenospheric depth, flows of PHMP material around plumes tend to be preferentially channelled along crustal weakness as ridges, and the intensity of flow along these directions is controlled in part by their spreading rates and prevailing stress and thermal fields. This does not preclude some PHMP radial transport beneath the plates from the hot plume centre. The intensity of such "radial" flows will, however, be comparatively small. From mass continuity principles one can easily imagine complex counterflows of the more passive DLVL material toward sections of the spreading ridges far removed from any hotspot centre, for example, south or 60°N along the narrow elevated part of the ridge.

Contrary to earlier views[61], the model implies that plumes are transporting to the Earth's surface a more primordial mantle material(s) than present in the low velocity layer lying beneath those mid-ocean ridge segments remote from plume. The upper few hundred kilometres of the Earth's mantle would therefore have been drained of large ionic lithophile elements and low-melting fractions during geological time to generate continents; the more primordial mantle richer in these elements and volatiles would lie deeper in the Earth, accumulating with time radiogenic isotopes and heat, thus leading to upward convection.

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Archaeological Occurrences of Early Pleistocene Age from the Shungura Formation, Lower Omo Valley, Ethiopia

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Stone artefacts have been excavated from stratified contexts in the upper members of the Shungura Formation. One occupation site and several secondarily-derived concentrations of artefacts were found. Potassium-argon age determinations for these occurrences indicate an age of approximately 2.0 million years. The artefacts recovered offer a contrast to those known from Lower Pleistocene deposits at Olduvai Gorge, Tanzania, and from still older deposits east of Lake Rudolf in Kenya.

ARCHAEOLOGICAL sites have been found stratified in Lower Pleistocene deposits in the Omo Valley. This is an important addition to the limited number of Plio-Pleistocene localities which have yielded artefacts, fauna, hominid remains and radiometrically datable materials. The only other notable occurrences in this time range are those of Olduvai Gorge, Bed I[1] and east of Lake Rudolf, Kenya[2].

Stratified concentrations of artefacts in derived contexts were first located in the Shungura Formation in 1971 by two of us (J. de H. and F. C. H.). These occurrences, designated FtJi1 and FtJi3[3], are in fossil localities 204 and 208 within Member F (previously localities 204, 206-208 were assigned to Member E[4]). Subsequently a programme of excavation and intensive survey undertaken (by H. V. M.) in 1971 and 1972 led to the location of a possible occupation site (FtJi2) in locality 396 in Member F. This report summarizes: (1) the stratigraphy and geochronology of known archaeological occurrences in the Shungura Formation; (2) the specific features of the two sites so far excavated; and (3) the characteristics of the artefact assemblages.
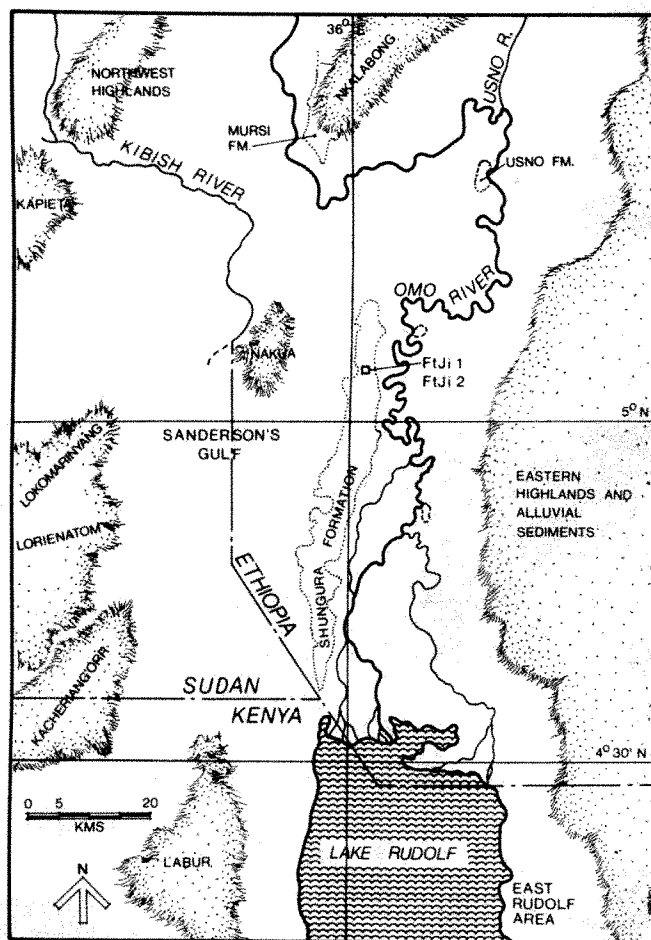

Fig. 1 Generalized map of the lower Omo basin, southern Ethiopia, indicating the locations of Plio-Pleistocene exposures. Highlands are stippled.
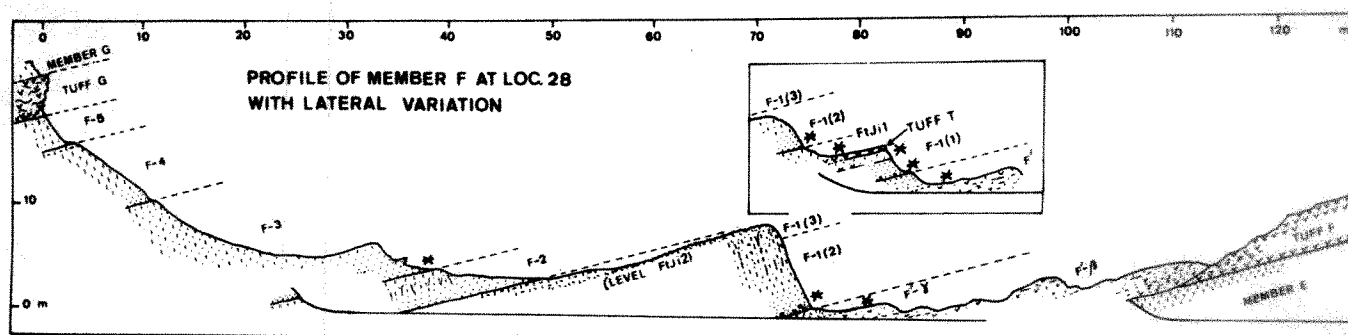
Fig. 2 Profile of Member F at locality 28, near the FtJi2 occurrence. The inset profile indicates the relative stratigraphical position of the FtJi1 occurrence.

Archaeological Occurrences

The Shungura Formation has an aggregate thickness of more than 700 m and a surface area of exposure of about 200 km². A series of K/Ar age determinations suggests that the base of the formation is older than 3.75 m.y.[4], and the top is somewhat younger than 1.4 m.y. (personal communication from F. H. Brown). The formation has been divided into ten members on the basis of nine widespread volcanic tuffs, designated Tuffs A through J. Each member, except the Basal Member, is composed of a principal volcanic tuff and the overlying series of sediments up to the base of the next principal tuff. The sediments of Members A through lower G are primarily fluvial, and the sediments of middle Member G and above are generally prodeltaic and lacustrine.

The lower members, Basal Member through Member E (roughly 4 to 2 m.y. old), have not yet yielded stone artefacts or occupational surfaces *in situ* in completely unambiguous situations. J. Chavaillon has reported the finding of a chopper in an outcrop of Member E, but subsequent excavation did not reveal any associated concentration of other artefacts[5]. Other occurrences of artefacts, none of which is definitely attributable to occupational surfaces, were found between 1968 and 1971 by two of us (J. de H. and F. C. H.) in sediments and tuffs of Member D and in channel situations in Member C[6]. At these occurrences the artefacts were found on the surface in situations which suggest that they originated from Shungura Formation deposits, but positive proof of this origin is lacking.

Thus far Member F deposits contain the oldest stone artefacts which are definitely *in situ* and the oldest artefacts associated with occupational surfaces. Occurrences in Member F have been found in two separate areas approximately 2 km apart in the northern outcrops and two other sites have recently been located in the southern outcrops (personal communication from J. Chavaillon). Isolated *in situ* artefacts have also been excavated from channel gravels in lower Member G, and other occurrences still to be studied have been found eroded from this member. No archaeological occurrences have been located in the uppermost lacustrine members, H, I and J, of the Shungura Formation.

Stratigraphy and Geochronology

Member F has a measured thickness of some 35 m of fluvial and floodplain sediments. Tuff F, at the base of the member, usually varies between 4.0 and 4.5 m but may attain a maximum thickness of 7 m. The average of two K/Ar age determinations for Tuff F gives an age of 2.04 ± 0.10 m.y.[4]. Overlying Tuff F are four to five cyclic units of fluvial and floodplain sedimentation. Each unit is usually composed of a graded sequence of coarse sands passing upwards through medium and fine sands to silts and clays. Occasional weakly developed palaeosols occur on the top of some of the silt and clay subunits within the individual cyclic units. The lowest unit in Member F, F-1, contains a widespread minor tuff, Tuff T. Fig. 2 illustrates the nature and variation of the sedimentary sequence near the FtJi2 occurrence and the relative stratigraphical positions of

the FtJi1 and FtJi2 occurrences within Member F. Tuff G which directly overlies Member F has yielded a K/Ar age determination of 1.93 ± 0.10 m.y.[4].

The FtJi2 Occurrence

The FtJi2 occurrence in locality 396 appears to be a primary context occupation site. The site is presently being dissected by the erosion of a small spur of fluviatile sediments in fossil locality 396. Thus far a small excavation of 2 × 5 m has recovered ninety-five artefacts *in situ*. The stratigraphical sequence at this locality is summarized in Fig. 3. The occurrence is a low density concentration of small artefacts scattered in a lens 12 to 15 cm thick, situated about 130 cm above the base of subunit F-1(3) (Fig. 3). The artefacts, almost entirely small fragments of shattered quartz lumps and pebbles, are the only stone fragments in the entire 2.5 m thickness of clay forming the lower half of subunit F-1(3). The artefact-bearing horizon has not yielded bone at this locality, but fossil pollen is preserved (personal communication from R. Bonnefille). The excavation has not yet determined the areal extent of the occurrence. The surface scatter of artefacts along the adjacent erosion exposure suggests a maximum north–south extension of about 20 m, but the east–west extent of the occurrence cannot yet be determined.

That the initial concentration of the artefacts was the result of hominid activity and that the occurrence can be considered an occupation surface is suggested for the following reasons. First, the artefacts occur in a very localized vertical and horizontal concentration in a clay deposit in which stone fragments and pebbles are otherwise totally lacking. Their physical condition is invariably fresh so that the possibility that these artefacts could have been selectively transported, concentrated and deposited in these sediments can be eliminated. Second, quartz lumps, small cobbles and their shattered fragments are generally extremely rare in even the coarsest gravels of the Member F deposits. This suggests that quartz is an exotic raw material introduced into the deposits from sources at least several kilometres distant. Thus only hominid activity
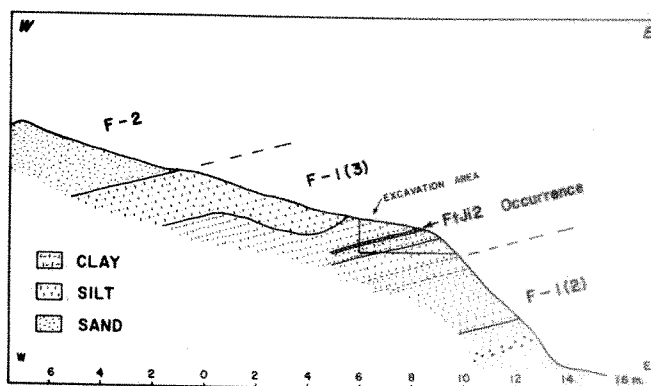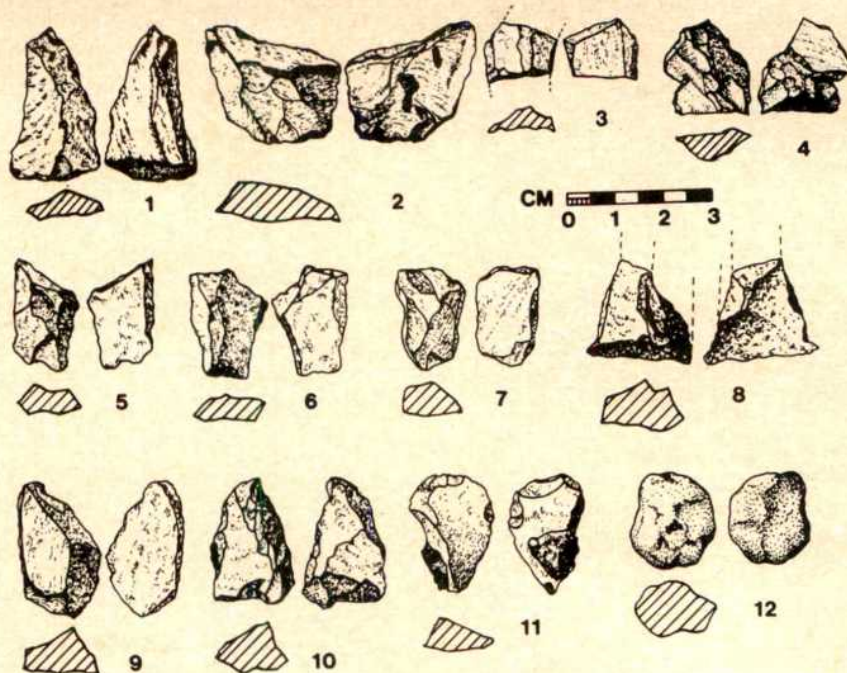

Fig. 3 Profile of Member F at locality 396 and the FtJi2 occurrence.

Fig. 4 *In situ* quartz artefacts from the FtJi2 occurrence. Flake fragments (1–2), angular fragments (3–11), and small pebble (manuport) (12).

can feasibly account for the localized presence of the quartz artefacts in the fine clay sediments.

It is not yet possible to reconstruct the detailed environmental setting of this occurrence. Stratigraphical studies (by J. de H. and P. H.) suggest, however, that initially the artefacts were scattered on a temporary land surface of silty clay in a backswamp or in a marginal flood basin situation. Subsequently, continued deposition under backswamp conditions buried the site. As a result of both the secondary development of a calcium carbonate concretionary horizon and the location of the site in clays which are subject to marked swelling and shrinkage with wetting and drying, all traces of the original temporary land surface have been obliterated. Undoubtedly this has slightly disturbed the scatter of artefacts and may account in part for their vertical dispersion.

The FtJi1 Occurrence

Fig. 5 shows the distribution of surface artefacts near fossil localities 204-208 and 215. There are six small (± 25 km^2) patches of densely concentrated artefacts in the 500×100 m area included in these localities. Furthermore, the entire locality 206–207 area is covered by a low density scatter of artefacts. These surface occurrences are almost entirely small quartz artefacts. The position of the artefacts at the base and

on the steep slopes of freshly eroded exposures makes it almost certain that most of them were recently eroded from Member F sediments. The absence of exposures of the Kibish Formation (of late or post-Pleistocene age) overlying the Shungura Formation in this area largely excludes the possibility that these discrete patches of artefacts could derive from geologically recent sediments. Moreover, each occurrence is associated with eroded exposures of a small stream channel which has been shown by excavation in locality 204 (the FtJi1 occurrence) to contain artefacts *in situ*. It is highly probable therefore that most of the artefacts in these surface scatters are of Member F age.

The FtJi1 occurrence in locality 204 was tested by an excavation of 2×4 m. A total of 130 artefacts and probable artefacts was recovered *in situ* from a small lens of sands and gravels, approximately 30 cm thick, filling the base of a small meandering channel. This channel is stratigraphically some 6 to 8 m below the FtJi2 occurrence and is situated at the base of the F-1(2) subunit (Fig. 2, inset profile). Mammalian fossils, including elephant, hippopotamus and several species of bovids, were also found. The artefacts appear to be in a secondarily-derived context; they were found in the gravel lenses of the channel fill and their physical condition varies from fresh to heavily abraded. The fossils also appear to be in a derived context, for they vary in condition from unrolled to

Fig. 5 Location of FtJi1 and FtJi3 occurrences and surface artefact scatters in the locality 204–208 and 215 area. Locality boundaries are shown with dashed lines.
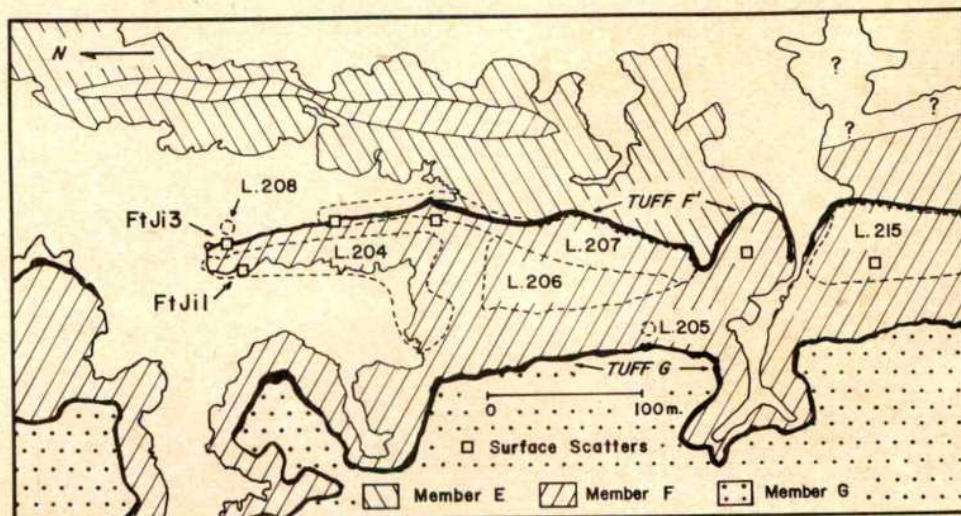
Table 1 Artefacts Recovered in the FtJi1 and FtJi2 Excavations

Artefact category	FtJi1 Excavated—1971			Surface (quartz only)		FtJi2 Excavated		Surface	
	Quartz	Lava	Chert	1971	1972	1971	1972	1971	1972
Debitage									
Flakes	11	—	—	17	2	1	2	2	3
Flake fragments	4	1	—	29	1	—	2	10	3
Angular fragments	107	1	6	197	11	11	77	52	23
Manuports	—	—	—	—	—	—	2	1	—
Total artefacts	122	2	6	257		95		94	
Range of maximum length (mm)	7–39	19–55	9–17	10–64		5–32		8–40	
Mean maximum length (mm)	16.0	—	12.7	24.8		13.4		20.4	
Distribution of maximum length (mm)	%					%			
1– 5	—					1.1			
6–10	18.9					38.9			
11–15	38.0					30.5			
16–20	23.7					12.6			
21–25	13.1					10.5			
26–30	4.9					4.2			
31–35	2.5					2.1			
36–40	0.8					—			
41–45	—					—			

heavily rolled. This suggests that both artefacts and fossils were concentrated in and deposited as part of the bed load of the stream. As numerous channel fills in Member F contain abundant mammalian fossils but lack artefacts, the presence of both artefacts and fossils in this channel may be fortuitous. Any postulated association between the artefacts and fossils, due to hominid activity before their incorporation into the channel deposits, is problematical.

Stratigraphical studies are inconclusive as to the original surface(s) from which the artefacts are derived. They may have been derived from primary contexts on the channel banks and flood basins adjacent to the small channel. The FtJi2 occurrence would be an example of a primary context site in a similar situation. It is also possible that the artefacts may have been preferentially discarded on the sandy substratum of the dry stream channel and subsequently reworked into the bed load of the stream. A pattern of preferential tool discard in channel situations such as this has been noted for the early sites east of Lake Rudolf[2].

Artefact Assemblages

The artefacts recovered in the FtJi1 and FtJi2 excavations and from the adjacent surface scatters are recorded in Table 1. A selection of the excavated artefacts from FtJi2 is illustrated in Fig. 4. The artefacts recovered from both sites are predominantly of milky white vein quartz. Most of them are small angular fragments of shattered pebbles and lumps of stone. Large core tools, such as choppers, and large artificially introduced unmodified natural stones (manuports) are not present in any of the excavated or surface samples. The size of the artefacts recovered in both excavations is small (see Table 1). The mean maximum length of quartz artefacts from FtJi1 is slightly longer (16 mm to 13.4 mm) than that of FtJi2. The frequency distribution of maximum length indicates that there are significantly fewer very small artefacts at FtJi1. This may be attributable in part to size sorting by stream action during deposition at FtJi1.

Most of the quartz artefacts from both occurrences are fragments of shattered quartz lumps. Whole flakes and flake fragments (pieces with a part of the bulb of percussion remaining) are rare. Pieces exhibiting intensive secondary retouch are absent. Several excavated pieces from FtJi2, however, show minor traces of edge damage, perhaps caused by utilization. These quartz artefacts can probably be interpreted best as the debris resulting from the intensive smashing of small quartz lumps and pebbles.

In the FtJi1 excavated sample there are two lava artefacts—one a split flake and the other an angular fragment. There are also six possible chert artefacts. All six are very small angular fragments and are slightly abraded. Small chert pebbles occur with moderate frequency in the stream channel deposits so that it is possible that these were produced naturally.

The artefact density of 9.5 artefacts per square metre on the FtJi2 occupation surface is low compared with most of the Lower Pleistocene occurrences at Olduvai Gorge[1]. It is fairly comparable to the low densities of artefacts recorded from the early sites east of Lake Rudolf[2], particularly because the ideal depositional conditions at the FtJi2 occurrence and the recovery techniques used allow the recovery of minute fragments which increase the apparent density of artefacts.

By comparison with the early archaeological occurrences known from Olduvai Gorge and from east of Lake Rudolf, the most notable features of the Omo occurrences are the absence of large tools, such as choppers, the preponderance of quartz as a raw material, and the generally smaller size of the artefacts. Although part of these differences may relate to different activity facies, at least part may be explained by the nature and proximity of the available raw material. Member F sediments are almost totally lacking in suitable raw material for tool manufacture. A tentative palaeogeographical reconstruction of the lower Omo basin for this time suggests that the principal outcrops of lava and quartz may have been 20 to 30 km distant. The nearest source of raw material probably would have been in stream channels several kilometres distant. These channels, draining the highlands forming the eastern margin of the valley, would have provided only small quartz lumps and pebbles for raw material.

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Genetic Apparatus of *Stylonychia* sp.

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The course of DNA changes during the formation of a macronucleus from a micronucleus in *Stylonychia* is followed.

Stylonychia sp. is a common ciliated protozoan with a genetic apparatus that makes it unusually useful for the study of the structure and function of the eukaryotic chromosome. *Stylonychia* is a hypotrichous ciliate, and preliminary evidence indicates that the phenomena described here hold for all hypotrichs, for example *Euplotes*.
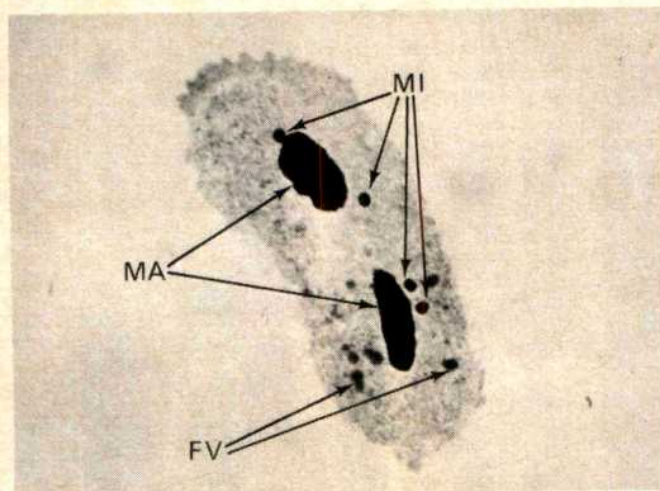

Fig. 1 A *Stylonychia* stained with the Feulgen technique and with fast green. The two macronuclei (MA) and four micronuclei (MI) are visible. The cell contains a few food vacuoles (FV) that stain with fast green.

Each *Stylonychia* cell contains four genetically identical, diploid micronuclei and two macronuclei that together contain about 600 times more DNA than a single diploid micronucleus (Fig. 1). Conjugation follows essentially the same plan as in other ciliates. The micronuclei of each conjugant undergo meiosis to form haploid nuclei. The cells exchange a haploid nucleus, and the exchanged nucleus fuses with a resident haploid nucleus to form a new diploid micronucleus. During this process, the old macronuclei and remaining haploid micronuclei are destroyed. The new micronucleus divides twice, producing four diploid micronuclei. Two of the nuclei remain as micronuclei, one is destroyed, and the fourth, the macronuclear anlage, is converted into a new macronucleus. Finally, the two micronuclei and the newly formed macronucleus divide in the absence of cytokinesis to produce the nuclear constitution of the vegetative cell.

The development of the macronuclear anlage is accomplished by a sequence of changes in the DNA. Ammermann[1]

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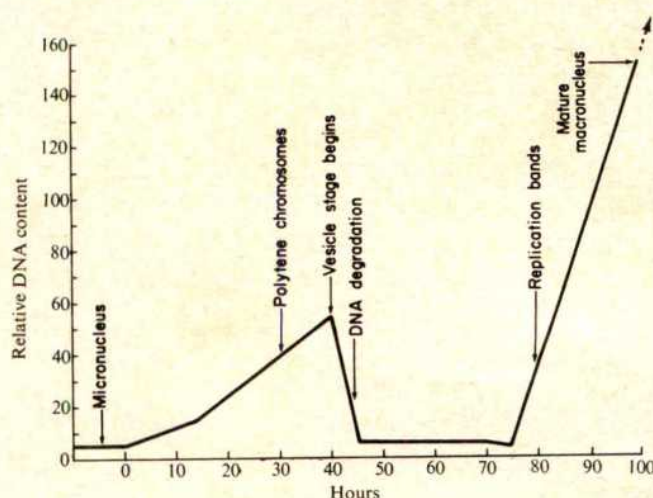
Fig. 2 The course of DNA changes during the development of the macronucleus from a micronucleus. The initial DNA build-up results in the formation of polytene chromosomes. The polytene chromosomes are cut into individual bands, and most of the DNA is then degraded. Finally, the remaining DNA replicates many times to produce the mature macronucleus. Modified from Ammermann[2] with permission.

has described the course of DNA increase that occurs as a micronucleus is converted to a macronucleus. These DNA changes are shown in Fig. 2, originally published by Ammermann[2]. The micronucleus that becomes the macronuclear anlage increases its DNA content approximately sixteen-fold, and in the course of this increase polytene-like chromosomes are formed. Soon after their formation, the polytene-like chromosomes are destroyed, beginning with the appearance of membraneous partitions between all the bands or chromomeres (Fig. 3a and b)[3]. The process continues such that each chromosome band becomes completely enclosed in a physically independent membrane-bound vesicle[1] (Fig. 3c). In summary, the macronuclear anlage is converted from a bag of polytene-like chromosomes to a bag of thousands of vesicles, each containing the material from a single band and parts of the two adjacent interbands. Nothing is known about the mechanism by which the chromosomes are cut up into separate bands or chromomeres. The transectioning occurs in the interband regions and at some stage presumably involves a double stranded endonuclease, the action of which is restricted to the interband DNA.

The splitting up of the chromosomes is followed by a reduction of 93% of the DNA to acid-soluble products, probably nucleotides[4]. After the destruction of DNA the vesicles disappear, and the remaining 7% of the DNA is more or less evenly distributed throughout the macronuclear anlage. A few hours later this remaining DNA goes through many rounds of replication, each taking place by means of the replication bands that are characteristic of hypotrichous ciliates. The DNA content increases to approximately 600 times the amount

BOOK REVIEW SUPPLEMENT

Biomedical Book Reviewing

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THE rapid proliferation of publications in the biomedical fields creates a great need for a constant, systematic, and critical selection of current biomedical literature. Because biomedical research is multi-disciplinary, book reviews have become primary tools in the selection and evaluation of biomedical titles. Reviews "which throw light on a work from the various interlocking fields can point the way from an indiscriminate mass of scientific writings to scientific literature. When critical judgments are pooled and receive bibliographic recognition over a sustained period, it becomes apparent that such collective criticism tends to sift and to lift out the works that are substantial, articulate and mature[1]".

For the most part, book reviews appear in subject journals, so in order to determine the current status of biomedical reviewing, I conducted a study of 285 general biomedical journals held by the Science Library at the Massachusetts Institute of Technology. Fifty-four English journals, which include *bona fide* book reviews, were selected. Detailed statistics were taken of books reviewed in all 1970 issues of these fifty-four journals. The book titles were checked against the "Weekly Record" section of *Publishers' Weekly, Forthcoming Books* and other pertinent sources to determine precise publication dates. Here I present a summary of those findings which seem to be of greatest interest to biomedical and other scientific researchers. No attempt is made in this article to describe the methodology of the study. Papers describing and discussing the project in much greater detail are planned for later publication in a library journal. It is possible to identify the principal biomedical book reviewing journals in terms of their quantitative coverage of reviews, point out the duplication patterns in book reviewing among these sources, and explore the effectiveness of these media in terms of speed of reviewing, comprehensiveness of review treatment, and authority.

The statistical results of this study of biomedical book reviewing reveal that there were 3,347 reviews of 2,067 biomedical books in the fifty-four journals in 1970 (Table 1). A reasonable approximation of the annual biomedical book output (including imports) in 1969–70 in the United States is about 2,300 titles (ref. 2 and C. C. C., in preparation), so the statistics suggest that quite a high proportion of these books (approximately 70%) were reviewed at least once in the fifty-four journals studied.

Table 1 also reveals that many books originally published in Britain and reviewed in the media (77.4%) were either reprinted or distributed in the United States by American publishers. Williams and Wilkins of Baltimore seems to be most active in this context. The 1,674 books available in the United States and reviewed in the media were either published or reprinted and distributed by 161 American publishers and/or distributors. The top three publishers alone accounted for 443 titles (26.46%) of the 1,674 books. They are, in decreasing order of activity, Williams and Wilkins of Baltimore, C. C. Thomas of Springfield, Illinois, and Academic Press of New York.

Fourteen journals accounted for 72.3% of all the reviews

Table 1 Statistical Summary of Biomedical Book Reviews Appearing in the Fifty-four Journals Examined for 1970

No. of reviews	No. of books
2,393	Of 1,370 books originally published in the United States
604	Of 354 books originally published in Great Britain (274 of these were either reprinted or distributed in the United States)
350	Of 343 books originally published in countries other than USA and Great Britain (mostly in languages other than English) (30 were either reprinted or distributed in the United States)
Total 3,347	Of 2,067 books (1,674 of which were available in the United States)

that appeared in the fifty-four periodicals examined for 1970. Details of the extent of review coverage in these journals will be found in Table 2.

Of the 2,067 titles reviewed in the fifty-four journals in 1970, 727 (35.17%) were reviewed in more than one journal. Of these, 420 were reviewed twice, 162 three times, and the rest (145 titles) four to eleven times. These 727 titles accounted for 2,007 reviews (59.96% of the total of 3,347 reviews). Only three of the fifty-four periodicals studied did not contain any reviews of these 727 books. Although these 2,007 reviews are scattered among almost all journal titles studied, the fourteen journals listed in Table 2, column 2, proved most likely to contain reviews of frequently reviewed titles, accounting for 1,576 (or 78.52%) of the 2,007 reviews of the 727 titles.

A random check of every third title of the 727 books was made to determine the duplication pattern in book reviewing among journals that have a tendency to review titles also reviewed elsewhere. The following interesting overlap results were obtained: about 35%—*Brit. Med. J.* and *Lancet*; 30%—*Ann. Intern. Med.* and *Arch. Intern. Med.*; 16%—*Lancet* and *Ann. Intern. Med.*; 15%—*J. Amer. Med. Assoc.* and *Lancet, J. Amer. Med. Assoc.* and *Brit. Med. J., J. Amer. Med. Assoc.* and *Ann. Intern. Med., J. Amer. Med. Assoc.* and *New Engl. J. Med.*

In the field of medicine, as in other areas of science and technology, currency of information is particularly crucial to researchers. "The success of any book selection tool would be in direct ratio to the time lapse between the publication of the book and its evaluation"[3]. The present study shows that the time lags among the fifty-four journals varied very widely, ranging from a mean of 5.8 months after publication for *Lancet* to 42 months for *Acta Radiol. Ther.* A rank list of the fifty-four periodicals studied, in ascending order of average time lag, was compiled. Some journals, such as *J. Dairy Sci.* and *Canad. J. Genet. Cytol.*, although relatively speedy in reviewing, are insignificant as selection media because of their small quantitative review coverage of the literature. Therefore, the list of highest ranked journals in terms of speed of reviewing

Table 2 Rank List of the Top Fourteen Biomedical Reviewing Journals in Terms of X, Y, and Z

	X (Quantitative coverage: No. of book reviews)		Y (Quantitative coverage: No. of reviews of the 727 books reviewed more than once in 1970)		Z† (Time lag)	
	Title	No. of reviews	Title	No. of reviews	Title	Mean time lag (months)
(1)	* Brit. Med. J.	375	* Brit. Med. J.	244	* Lancet	5.8
(2)	* Lancet	317	* Ann. Intern. Med.	215	* Brit. Med. J.	6.6
(3)	* Ann. Intern. Med.	277	* Lancet	204	* J. Amer. Med. Assoc.	7.2
(4)	* J. Amer. Med. Assoc.	260	* J. Amer. Med. Assoc.	168	Brit. J. Haematol.	7.2
(5)	Arch. Intern. Med.	211	Arch. Intern. Med.	138	J. Bone Joint Surg. (GB)	8.6
(6)	* New Engl. J. Med.	174	* New Engl. J. Med.	121	* New Engl. J. Med.	8.8
(7)	Quart. Rev. Biol.	155	Quart. Rev. Biol.	80	Clin. Pharmacol. Ther.	8.9
(8)	Bioscience	123	* Canad. Med. Assoc. J.	72	* Yale J. Biol. Med.	9.3
(9)	* Canad. Med. Assoc. J.	116	* Arch. Pathol.	65	* Ann. Intern. Med.	9.6
(10)	Amer. J. Med. Sci.	102	Amer. J. Med. Sci.	63	* Canad. Med. Assoc. J.	9.8
(11)	* Gastroenterology	91	* Gastroenterology	59	* Arch. Pathol.	10.2
(12)	* Arch. Pathol.	89	Bioscience	55	* Radiology	10.2
(13)	* Yale J. Biol. Med.	67	* Yale J. Biol. Med.	52	* Gastroenterology	10.4
(14)	* Radiology	63	* Radiology	40	Brit. J. Radiol.	10.5
	Total 2,420		Total: 1,576			
	(72.3% of the grand total of 3,347 reviews)		(78.52% of the 2,007 reviews of the 727 books)			

* Titles appear in all three columns.   † Journals containing fewer than twenty reviews in 1970 were ignored.

(Table 2, column 3) includes no journal that reviewed fewer than twenty books in 1970. It is encouraging to find that several periodicals rank high in terms both of coverage and speed of reviewing as indicated in Table 2.

Detailed statistics of time lags for all 3,347 reviews were also collected (Fig. 1). Clearly there is a very wide range of time lags in biomedical book reviewing, ranging from reviews coinciding with the date a book came off the press (0 month) to that appearing 108 months (9 yr) after publication. The highest number of reviews appeared around 8 months after the books with which they dealt were published. Simple calculation yields a mean time lag of 10.43 months ($\bar{T}_1$) for all 3,347 reviews and a standard deviation of 6.63 months (σ). This means that a review of a biomedical book will most probably (68% confidence) be found within the time limit imposed by 17.06 months $< T_1 < 3.8$ months.

I made no attempt to study the quality of each book review. Nevertheless, the average review length (number of words) of each journal was computed. This can be a fair indication of the degree of comprehensiveness of review treatment in each journal. It was generally found that journals with longer time lags in reviewing tended to be the more scholarly periodicals and to provide longer reviews (with an average length as long as 865 words). The highest ranking fourteen journals from the standpoints of coverage and promptness were found

to include much shorter reviews (with an average length of about 350 words).

Of the fifty-four journals studied, only three titles, Lancet, Brit. J. Haematol. and Canad. Med. Assoc. J., do not have signed reviews, and all these appeared among the highest ranking fourteen journals for coverage and promptness of reviewing.

It is obvious from this study that many biomedical reviewing journals can be disregarded by researchers and librarians for selection purposes because of the limited number of titles covered by their reviews and their comparative sluggishness. On the other hand, one can easily identify from Table 2 those reviewing media most likely to be useful for selection.

Considering that many scientific books are already out of date before they are published, it should be stressed here that an unreasonable time lag in reviewing is a very serious problem in terms of book selection and evaluation. This study showed that although many reviews meet high standards of criticism and evaluation, they are of little value in selection because they do not appear promptly enough. Earlier studies have shown that, on the average, book use declines most rapidly in the early years following publication—about one third of a scientific book's usage is in its first year after publication and half in its first three years[4]. If therefore a library book order were generated from a review which had a time lag of 6 months, library readers would not be able to use that book until at least 9 months or a year after its publication. One third of this book's life would then have passed.

It seems reasonable to suggest that if reviews are to be useful for medical book selection, the time lag between the publication date of a book and the appearance of a review ought not to exceed 3 or 4 months. At present, all journals studied clearly are far from meeting this modest goal. It is, however, one toward which all editors of journals, reviewers, book publishers, and librarians and researchers who use the reviews should work collectively and diligently.

[1] Bry, I., and Afflerbach, L., Mental Health Book Review Index, 8, iv (1963).
[2] The Bowker Annual of Library and Book Trade Information, 70 (Bowker, New York, 1971).
[3] Runser, R. E., in Proc. Tenth Inst. Public Library Management, 43 (University of Wisconsin, 1965).
[4] Morse, P. M., Library Effectiveness: A Systems Approach, 89 (MIT Press, Cambridge, Massachusetts, 1968).
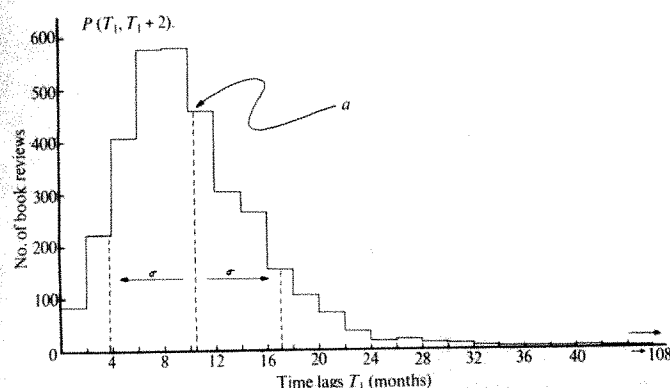

Fig. 1 Histogram of time lag distribution for 3,347 book reviews. a, $\bar{T}_1 = 10.43$ months (mean time lag for 3,347 book reviews). σ (standard deviation) = 6.63 months.

General Books

Bridging the Culture Gap

Science for Non-Scientists: An Examination of Objectives and Constraints in the Presentation of Science to Non-Specialists. By J. S. R. Goodlad. Pp. x+169. (Oxford University: London, January 1973.) £3.25.

SUPPOSE that 40 per cent of our intelligentsia were accustomed to migrate to China at the age of 15. They make themselves quite at home there, and learn to speak and write the language fluently. Ten years later they return, and enjoy thereafter a sort of dual nationality, spending part of each year in Britain, as ordinary family men and women, but going back to China for weeks or months at a time to take their part, also, as citizens of that country. How could they best explain to the stay-at-homes what it is like to live in China amongst the Chinese?

One can imagine some of the methods that might be tried, and can easily guess their consequences. One group might give a general survey of Chinese geography ; this would prove very indigestible and uninspiring. Another institution might concentrate on the history of China, which would be interesting for those with a taste for history, but otherwise a little dry and academic. A very advanced and sophisticated teacher might attempt to discuss the current social problems of the Chinese people, but his listeners would find it difficult to relate this to the simple facts of Chinese society. The attempt to distil a few great thoughts and significant concepts out of Chinese philosophy would fail for lack of understanding of Chinese language. A practical course on how to make a Chinese junk would prove amusing, but not very relevant to the main purpose.

In the end, they would probably discover that the only useful thing to do is to invite their friends and relations to visit China themselves for a short time. They might suggest, for example, a short guided tour of one of the great cities, to be delighted and overwhelmed with the splendour of the ancient monuments and the delicacy of the Chinese cuisine. Others might prefer to spend a few weeks living in some quiet village, sharing the daily life of the peasants, helping perhaps to harvest the rice or to build a new farmhouse. The language barrier would still be an obstacle, but with skilled interpreters some modest dialogue might be achieved with the inhabitants: at least the tourists might

come to understand that these creatures were human beings and not goblins or mechanical robots, and that they lived

To make the most of such a programme, it would need to be integrated into the education system at all stages. In the primary school, for example, pictures of Chinese landscapes, little games to dramatize the Chinese way of life, and a few elementary lessons on Chinese ideograms would make children sympathetic to China and its people. Throughout secondary and higher education, this process should continue, so that every educated citizen would be familiar with Chinese ways of thought and action. Unfortunately, there are serious obstacles to this desirable reform. The very sharp segregation of the Sinologues preparatory to their migration, a peculiar feature of the British educational system, is often anticipated by several years; and those who do not emigrate learn practically nothing about China beyond this stage, and regard it as more fabulous than ancient Cathay.

Indeed, many people argue that the division should be much less definite, and those who go should continue to spend part of each of these formative years in their native land, and that the non-Sinologues should be made to visit China regularly in school parties or even as individual travellers. All these questions are now widely discussed, but nothing is done: schools and universities blame each other for impeding reform, but no common plan of action has been devised.

At the university level, also, schemes for bridging the gap between the two cultures are being tried out here and there, but without great success. Part of the difficulty is that China itself is a very large country: the Cantonese know little of Peking and the Tibetan plateau is very distant from the delta of the Yellow River. Provincial loyalties run

high and the honest simple-minded wanderer must argue his way through many artificial frontiers. The best results have been obtained with a programme of guided visits to selected areas but a whole extra year is regarded as too costly by the powers-that-pay. Perhaps not sufficient emphasis is laid on the exploration of certain common frontier areas: for, if we study *geography* we may observe that China begins, in truth, at Calais; and in the eyes of *psychology* all civilizations are one.

All these points are made thoughtfully, accurately, and with apt citation of many sources, in this excellent book. It is not very long or laborious, or does it pretend to great subtlety nor depth, but it analyses very shrewdly and positively one of the most serious and difficult problems of our present-day culture.   JOHN ZIMAN

Introductory Induction

An Introduction to Confirmation Theory. By Richard Swinburne. Pp. vi+218. (Methuen: London, January 1973.) £3.90.

STUDY of the logic of scientific systems involves problems of inference that are inductive as well as deductive and statistical. After a period of eclipse, the importance of inductive logic is now increasingly recognized, and there is a body of acceptable results and significant problems which is amenable to systematic treatment. Professor Swinburne gives such a treatment in introductory fashion in this book, which will provide a useful textbook for university courses in inductive logic and philosophy of science.

The problem of developing a confirmation theory should be distinguished from two other problems which it does not pretend to discuss. It is not, in the
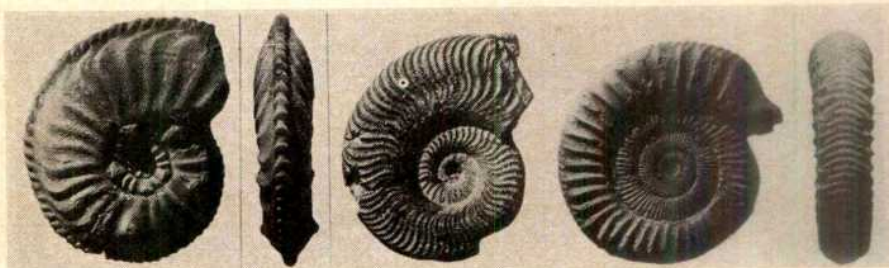
Typical Pliensbachian ammonites from Würtenburg, Germany. An illustration from the *Atlas of Palaeobiogeography,* edited by A. Hallam (Elsevier, Amsterdam, 1973).

traditional sense, a justification of inductive inference. Swinburne makes clear that he is rather drawing out "the criteria implicit in our ordinary judgments" of what it is to be a correct inductive inference. Neither is confirmation theory a theory of statistics, although the most fully developed confirmation theories have been based on relations of probability between evidence and hypotheses and predictions, and this is the approach Swinburne adopts. Calling these "epistemic probabilities", he compares and contrasts them with more familiar applications of the probability calculus in classical, frequency, logical, subjective, and propensity interpretations, and argues for the adoption of the probability axioms in epistemic contexts. This leads him to discuss some traditional problems of probabilistic confirmation theory, including Carnap's conclusion that all universal generalizations have epistemic probability zero, Hempel's suggested criteria of confirmation and his "raven paradoxes", Goodman's "grue paradox", and the question of probabilistic conditions for the acceptance of a hypothesis on given evidence. All these issues are discussed with accuracy and clarity, and often with original and illuminating twists which take them beyond mere recitals of the current literature.

Swinburne is aware that the general principles of epistemic probability he develops have so far been applied only to very simple examples of law-like generalizations, and not to more complex patterns of argument such as are found in scientific theories. Even an example of analogical argument that he hopes will be "more realistic" (namely "that all specimens of many types of acid have a certain property increases the probability that all specimens of another type of acid will have that property") is not, I think, fully justified by the confirmation principles he has adduced. Goodman's theory of "entrenchment", on which he depends, is not sufficient here, because this inference would be justifiable in scientific practice even before the word "acid" was entrenched in the language. Again the notion of "simplicity" is a very familiar one in scientists' own appraisals of their theories, but Swinburne's chapter devoted to this topic is mainly a discussion of the philosopher's rather parochial "grue" problem, rather than a general analysis of types of simplicity.

The book summarizes excellently the position now reached in the development of confirmation theory, but in so doing it reveals the inadequacy of current ideas to encompass more interesting features of scientific inference, and also it does little to indicate where the points of growth might be.

MARY HESSE

Aero-economics

Air Transport Economics in the Supersonic Era. By Alan H. Stratford. (Second edition, revised and extended.) Pp. xiv+506+8 plates. (Macmillan: London and Basingstoke, 1973. £10.

IT is unfortunate that a book about "the supersonic era in air transport" should come out just when that era is in danger of never getting started or at least of being postponed by ten or twenty years. When the first edition of this book was published in 1967 there were still four SST designs in the running—two American, the British and French Concorde and what was to become the Russian TU 144—and it was widely thought that there would be some 500 supersonic airliners operating in the late 1970s, more or less taking over from the B 707s and DC8s just as these had taken over from the old Stratocruisers and DC7s six years before. Since 1967 the two American SST designs have been abandoned, the estimated selling price of Concorde has escalated from £5 million (with some return on research and development cost) to over £20 million (with no return on a hugely inflated research and development cost), the wide-bodied aircraft have reduced subsonic seat-mile costs by 20 per cent (in real terms), and estimates of sales of SSTs have dwindled from 500 to about 25.

Technology may later learn how to build a supersonic airliner at a more reasonable price (and with more acceptable noise in take-off and landing) so that by 1985 or 1990 it may be possible once more to talk realistically of a supersonic era for air transport as a whole and not merely for a few VIPs in a hurry. In the meantime there are many other developments in air transport that require attention, not so glamorous as supersonic flight perhaps, but much more important both for the airlines and for the great mass of travellers, and Alan Stratford has added a great deal of useful material on these, which, if not factual and conclusive, at least points the way to proper study.

Most important in the immediate present are the sections on the development of jet transportation (chapter 4) and the extremely low fares offered for holiday travel first by the charter operators and soon on scheduled services, which have opened the door to the mass travel market. Using largely depreciated aircraft (or new wide-bodied aircraft) with maximum tourist seating and an 85 per cent load factor, the charter operator can cut 50 per cent off his "direct" or "aircraft" passenger-mile costs, and by wholesaling his seats he can cut his "indirect" or "ground" costs by as much as 80 per cent, thus being able to offer a fare some 65 per cent below the standard scheduled service fare. The market for holidays in the sun at these fares is enormous and the total figure of passenger-miles in world air transport (scheduled and non-scheduled) may well continue to expand at its old rate of about 14 per cent per year into the 1980s and beyond. The era that we are entering is not the era of supersonic air transport, but the era of mass air transport.

As before, Alan Stratford is perhaps most useful in those parts of his book on air cargo, where his personal experience is particularly wide. Unfortunately neither the low unit operating costs of the bigger jets nor the mechanization of ground handling, with its pallets, containers and computers, have so far led to the sort of break-through in freight rates that we have achieved in passenger holiday fares. World air freight volume is increasing, but airlines still complain that they lose money on their all-freight services and make a profit only from the supplementary revenue produced by cargo carried in the bellies of passenger aircraft (without this freight revenue, however, the scheduled passenger services would almost universally lose money).

The treatment of R/S/V/Q/TOL (reduced/short/vertical/quiet take-off and landing) is good in theory but perhaps over-optimistic in practice. We still await a V/TOL aircraft quiet enough for city-centre operation and yet large enough and fast enough to have reasonable economics in competition with wide-bodied conventional aircraft on the one hand and the high-speed passenger train on the other. As for R/S/Q/TOL aircraft, it is easy to see their advantages in reducing noise and runway congestion at airports, but difficult to persuade the airlines to buy them when their unit operating costs are significantly higher than those of conventional aircraft. Moreover all these attempts to develop air transportation to city centre or near city centre tend to be frustrated by urban traffic congestion. At many times of day it takes as long for a taxi to go from Park Lane to the Surrey Docks as to Heathrow. The helicopter service from the top of the Pan Am building in New York (and Wall Street), to Kennedy, La Guardia and Newark takes a quarter of the time of the airport bus or taxi, but attracts few passengers and regularly loses money. (It may be that the unbelievable rudeness of New York taxi drivers when asked to do a short down-town trip instead of fifteen miles to an airport has something to do with this.)

Alan Stratford has added substantial sections on cost-benefit studies of airport location, taking into account the extensive work of the Roskill Commission and the many studies of noise nuisance and its assessment that have taken place since the first edition of his

book. These and the biblographies at the end of each chapter will be found particularly useful to students of air transport even if the input figures and forecasts for the studies and the conclusions of the reports have proved to be unacceptable to the public and parliament.

A. M. Lester

Brain as She is Spoke

The Metaphorical Brain: An Introduction to Cybernetics as Artificial Intelligence and Brain Theory. By Michael A. Arbib. Pp. xii+243. (John Wiley: New York and London, September 1972.) £6.25.

"Distributed action-oriented computation in layered somatotopically organized machines . . . for now the reader need simply note that this will prove to be an important catch phrase in our brain theory." I will not say that this quotation from page 5 of Arbib's book sets the whole tone for what is to come, but it does provide a rather disturbing presage. The book is in three parts: an introduction, which includes a certain amount of basic neurophysiology and neuroanatomy, then a section on systems theory and artificial intelligence, and finally a discussion entitled "Brain Theory", much of which has to do with motor systems.

Arbib adopts the portentous declamatory mode, a style affected by a number of cyberneticians. To give another example: "We thus model LTM (long term memory) as *residing in the intervening network between sensory layers and motor layers*. It is represented in the parameters of the network which enable the array of sensory feature activation to be segmented and transformed into a spatially tagged array of OFCs" (the italics are Arbib's and an OFC we have been told previously is an output feature cluster, "the encoding of an object in the action frame, that is . . . a cluster of features that might be appropriate for interaction of the organism with the object"). He balances a fine line between tautology and obscurity, though continually giving a strong impression of the complexity of the mechanisms of the brain. This is not to say that the ideas he is discussing are not important—many of them are, and occasionally he succeeds in being illuminating about them. He is best when describing the action of particular computer programs, for instance, some of those that have been written for the Stanford and MIT robot projects, and also when he describes fairly well understood neurological mechanisms such as the gamma efferent control system of muscles. He surrounds these accounts, however, with a great deal of talk about redundant this, and

Fan Sculpture
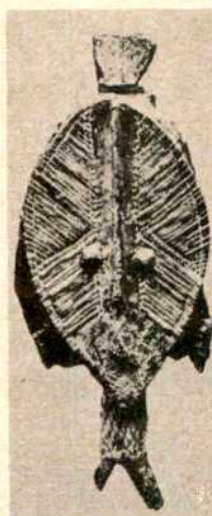
Example of Betsi, Ntumu and Mekeny carvings from the Cameroons. In *Statuaire Fan Gabon* (ORSTOM, Paris, 1972), Louis Perrois subjects the primitive art of this region to detailed morphological analysis.

integrated that, freely interleaved with assertions about hierarchically arranged representations of successively more sophisticated behavioural functions. One is reminded very strongly of the writings of Hughlings Jackson. Despite the new vocabulary of cybernetics, much else remains. As in Jackson, here is a set of potentially appealing ideas enveloped in a rather strange and diffuse style. What is more, many of these ideas, having to do with somatotopic organizations and hierarchies of successively more highly evolved neural representations in terms of patterns of action, together with the attempt to pin these down to neurological embodiments, are Arbib's subject matter, and

are exactly the concepts Jackson was wrestling with (though not always successfully) a hundred years ago.

What is required now in brain research is not just ideas juxtaposed in the hope that they will somehow organize themselves into understanding in the mind of the reader. We are in a position to spell out in some detail the formal structure of a few systems capable of supporting certain kinds of mental process. Artificial intelligence and systems theory provide some of the basis for this. It seems possible furthermore that the computer may be an appropriate vehicle for expressing and testing theories of brain mechanisms and mental processes. Brain research

and psychology might in that case be poised for an important conceptual revolution and for fundamental empirical advances. Arbib has selected some of the right general topics, and some of the right substantive material, and many of the ideas that he treats are both interesting and important. However, I have some doubt as to whether the degree of enlightenment he sheds will exceed the amount of mystification. This may seem rather harsh since many of these problems, because of their fragmentary development, are as yet very obscure. Maybe some of the issues which are raised here are too difficult to give any scientific account of at present, even though we can recognize their importance and can see occasional glimmerings of understanding here and there. In this case Arbib may well be justified in flying a few kites in an attempt to get people thinking.

Finally, it is impossible to resist the temptation to mention the quirk which has been adopted in this book of using exclusively the female form of third person pronouns: "it gives the reader all she needs in system theory", and so on. If Michael Arbib means this as a gesture of male solidarity with women's liberation she might have been more appreciated by members of that movement had she written a rather more comprehensible account.

KEITH OATLEY

History of Hydraulics

Hydraulic Power. By Ian McNeil. Pp. ix + 197. (Longman: London, November 1972.) £3.75.

In Mr Ian McNeil's book *Hydraulic Power*, one of the Industrial Archaeology Series edited by L. T. C. Rolt for Longmans, the author has had two objectives in view. His prime object has been to give a short account of the history of hydraulic power, beginning with the early inventors Pascal and Bramah, and progressing through Armstrong, Tweddell and Ellington to Hele-Shaw, Beacham, Constantinesco, Sinclair, Dowty and Ferguson to reach the present state of knowledge. From 1930 onward hydraulic power experienced a kind of renaissance, particularly through the development of nitrile rubber, a material with physical properties exactly fulfilling the requirements for seals and packings of hydraulic components. His second object is to survey this field for the industrial archaeologist.

The book covers a good deal of ground, dealing with a number of different topics that nowadays would be unlikely to be found together between two covers, even in a book on the history of energy. It is interesting to read, but lacks conciseness. It wanders from one subject to another. The chapter head-ings have no standard of parity, emphasizing this desultory treatment. Some of the illustrations are not very clear—for example, Armstrong's rotary hydraulic machine of 1838—whereas a few, such as that of Elisha Otis's safety lift, are quite fascinating.

A number of interesting schemes that have since been abandoned are considered—for example, Constantinesco's wave transmission. The most noteworthy sections include chapter 7, dealing with hydraulic mains systems, municipal and metropolitan, and drawing attention to the fact that a great many of these networks are still in existence and in daily use. Chapter 8, "Cranes, Hoists and Lifts", reminds us of the lead taken over by the USA in many large scale projects from 1866 onwards, which led to its primacy later in the mining and construction industries. Also interesting is the section on fluid coupling and torque converter (chapter 11), though here the description would be much clearer with the addition of a diagram. Chapter 12, "Twentieth Century Renaissance", pinpoints the part that many small improvements have played in this regard.

In promoting his second objective, the author has interpolated the views of the industrial archaeologist throughout the book, and has carefully described a great many of the earlier hydraulic machines, with their auxiliary apparatus, pumphouses, etc., many of which are still working, or have been preserved by museums or other agencies. He gives careful directions to sites where they can be seen, and a short gazetteer completes the book. This information is important and valuable, both as a record of the machines and as a welcome source of reference for the industrial archaeologist.

AUBREY BURSTALL

Moseley and the Elements

Moseley and the Numbering of the Elements. By Bernard Jaffe. Pp. x + 263. (Heinnemann: London, November 1972.) £1.50.

It is always interesting to ask what opinion the biographee would form of his biography. In this case one can, I think, be quite certain of the answer: Moseley would have held this work in contempt. Jaffe writes in his preface of "writing a full biography" and appends a "Complete List of Research Papers by Moseley"; he implies that he has spent ten years gathering material and thanks nearly thirty persons, including a score of Moseley's acquaintances, for aiding his researches; he has found in the archives and quotes at length (though not always in full) the known letters from Moseley to Rutherford, C. G. Darwin, and N. Bohr. But this material, which apart from the letters proves to be negligible, is then folded into a pabulum of romanticized science digested to gibberish for consumption by pre-adolescents. There are sections —for example that on the discovery of the diffraction of X-rays by crystals ("chapter 4. Moseley is Stirred by the Crystal Gazers")—which may be taken as veritable paradigms for wanton carelessness of factual accuracy and traduction of physical principles. This slough of confusion (as to genre and audience as well) was originally published as one of the paperbacks in the "Science Study Series" intended as supplementary readings for a distinguished American secondary school physics course. It here appears in its British edition between hard covers at twice the American price but without the collection of plates in the original.

In his preface Jaffe rues his failure to turn up the very extensive collection of letters which Moseley wrote to his mother and sister, recognizing perhaps that only they would give the record of Moseley's experiences, activities, and personality upon which an adequate biography could be based. But these letters have in fact come to light; together with Moseley's scientific correspondence they have now been edited and annoted by John L. Heilbron: *H. G. J. Moseley : The Life and Letters of an English Physicist, 1887–1914* (University of California Press, Berkeley, in the press). It is to Heilbron's scholarly study that anyone with a serious interest in Moseley and the numbering of the elements will have to turn.

PAUL FORMAN

Unifying Principles

Statistical Mechanics: New Concepts, New Problems, New Applications. Edited by S. A. Rice, K. F. Freed, and J. C. Light. (Proceedings of the Sixth IUPAP Conference on Statistical Mechanics.) Pp. viii + 423. (University of Chicago: London and Chicago, 1972.) £7.20.

The conference that brings active workers in related disciplines together is rightly becoming fashionable. We have here twenty-one papers ranging over statistical mechanics and the related fields of hydrodynamics and cybernetics given in March/April 1971. A glance at the list of distinguished contributors shows that it must have been very enjoyable indeed to listen to their interactions, some of the flavour of which has been preserved by recording the discussions after each paper. For example, it emerged that, rather disgracefully, very little is known in general about the limiting behaviour of equilibrium properties near absolute zero temperature, which is a little surprising when one considers all the work that has gone into studies of ground and low-lying states of particular systems.

Also that there is often very real doubt on how to choose "good" variables in particular problems.

The organizers, rightly in my view, have a horror of parallel sessions. For time-table purposes, there were five successive sections: "Fundamental Principles", "Developments in Biology", "Generalized Hydrodynamics" (including turbulence), "Phase Transitions" and "Liquids", the papers being printed in the order in which they were actually given. (In fact, there was a great deal of overlap between the sections.)

The papers are all of a high standard and many of them will be valuable for a long time to come as review articles, but it would be quite wrong to conclude that anyone was merely "doing his own thing"—it is absolutely clear that everyone had other fields very much in mind. For example, there are very interesting discussions of the concept of a limit cycle. This is fundamental in mechanics, in turbulence and in neural networks, yet ergodic theory has gone to great pains to try to show that no such thing occurs

(or that it can be negected as "exceptional" if it does) in the "ordinary" systems studied in statistical mechanics. Another very interesting general concept is that of static or dynamic scaling. The consensus here is that there is "a great deal in it", even though very little can be rigorously proved at present.

The book has been produced by photographing typescript on to very good paper: the result is easy and pleasant to read. I certainly recommend it to any serious worker in any of these fields.   H. N. V. TEMPERLEY

Physical Sciences

J. A. Wheeler

Magic Without Magic: John Archibald Wheeler. Edited by John R. Klauder. Pp. xiii+491. (W. H. Freeman: San Francisco and Reading, January 1973.) £9.20.

THIS volume contains the *Festschrift* collected to honour J. A. Wheeler on his sixtieth birthday. In it a galaxy of physicists has contributed essays on topics to which Wheeler has made important contributions. Many photographs are inserted at various places in the book and the volume starts with an introduction in which a number of people give their impression of Wheeler: one of the executives of DuPont describes Wheeler's impact on the work at DuPont for the Manhattan Project to design a plutonium manufacturing plant; Teller describes Wheeler's contribution to the hydrogen bomb project, and Spitzer his work on Project Matterhorn; the chairman of the Princeton Physics Department, one of the Trustees of the Batelle Memorial Institute, and the Director of Institute Research in Physical Sciences of the Batelle Memorial Institute recall Wheeler's contributions to easier communication between scientists and politicians; finally, the President of Stony Brook tells about some of Wheeler's work in the early days of particle physics. This introduction gives an excellent impression of Wheeler, the physicist and man; it is complemented by the last essay, "The Anatomy of Collaboration", by E. F. Taylor who wrote with Wheeler the introductory relativity textbook *Spacetime Physics*.

The essays between the introduction and Taylor's essay are original scientific articles stemming in one way or another from the authors' association with Wheeler (to quote from the preface). The first two essays deal with the deformation of nuclei—studied in

the classic Bohr–Wheeler and Hill–Wheeler papers—and the related problem of the existence of superheavy nuclei. The next two essays consider mesic atoms, a topic broached by Wheeler in 1949. Wheeler and Feynman considered retarded and advanced effects in 1949; this subject is taken up by Synge in an essay on the electrodynamic double helix. Then follows an essay on retarded long-range interaction potentials between molecules—a topic treated by Wheeler in 1941.

It is not generally known that although Heisenberg coined the expression S-matrix in 1943, the concept of a collision matrix, that is, a way of characterizing a collision process by specifying the ultimate state of the system was introduced by Wheeler in 1937. Two essays, by Goldrich and Wigner and by Regge, consider the properties of the S-matrix. As Wheeler himself has shown the power of what Maxwell called the "cross-fertilization of the sciences", it is fitting to find in this *Festschrift* an essay describing experiments to test various aspects of relativity using, respectively, gyroscopic precession, nuclear electric dipoles, and superconducting flux quantization.

In recent years Wheeler's main interest has lain in the theory of relativity, covering such aspects as gravitational collapse, Mach's principle, superspace, geometrodynamics, and the quantization of gravitation. It is therefore not surprising to find that more than half of the essays are dealing with these and other aspects of the theory of relativity. Among the authors we find the Russian experts Zel'dovich, Khalatnikov, and Pokrovski, as well as Western specialists such as Penrose and Dicke, to name but two.

Altogether this volume provides the reader with a veritable feast, well worthy of the man in whose honour it was written.   D. TER HAAR

Solid State Chemistry

Preparative Methods in Solid State Chemistry. Edited by Paul Hagenmuller. Pp. xvii+602. (Academic: New York and London, December 1972.) $36.

SOLID state chemistry is not too well served with books. Because its subject matter overlaps with other disciplines, and the motive for much recent work has had a physical or technological basis, the relevant experimental methods are dispersed through a wide range of journals. The idea behind Professor Hagenmuller's book is therefore welcome.

What is involved is the study of phase equilibria, solid state reactions and the synthesis of pure materials, usually by high temperature methods. The combination of high temperatures with very high pressures has opened up much new chemistry, and the book starts well, with chapters on high pressure techniques (by Rooymans) and high pressure synthesis (from MIT Lincoln Laboratory, where it has become the standard procedure). There is also an uninformative chapter on Russian work using transient shock wave methods. Thereafter, the balance of the book is somewhat impaired by over-emphasis on crystal growing. Important as this is for technology, it is only one aspect of preparative solid state chemistry. Methods are reviewed, in relation to high-melting oxides, by Anthony and Collongues. It is to be regretted that they give only scanty, incidental attention to the techniques of high temperature experimentation, for Collongues and other French workers have done much work on reactions and phase studies above 2,000 K. A chapter on such methods would have enhanced the value of the book. The same deficiency on the side of high temperature technique detracts from the otherwise useful chapter, by Windisch

and Nowotny, on carbide chemistry. With other chapters on chemical vapour transport, synthesis by electrolysis of fused salts and fluorine chemistry, about two thirds of the book can be welcomed as a useful source of information to those working in or entering the field.

The remainder of the book is probably unduly specialized: preparation of single crystals of III/V semiconductors and of cadmium sulphide, preparation of ferrites, oriented eutectic crystallization and so on, together with a chapter on elementary boron which is remarkable for its complete failure to mention the curious metallic borides, of very high boron content, which so long masqueraded as the element itself. These topics are important for technology, but they overweight one facet of the subject and some of them have been repeatedly discussed in other books. One saving point is that the writers have used the opportunity to deal with the principles underlying particular problems.

The book as a whole emphasizes principles and objectives, as well as methods. The editor has managed to get his collaborators to cover the ground without much overlap or repetition — even though one diagram, of a hydrothermal bomb, does appear in two different chapters. The book is well produced— as indeed it should be, at the price.

J. S. ANDERSON

Atmosphere

Handbuch der Physik/Encyclopedia of Physics. Gruppe 10 : Geophysik, Band 49. Teil 4. Geophysik 3/Geophysics 3. Teil 4. Chief editor, S. Flugge. Edited by K. Rawer. Pp. vi+579. (Springer: Berlin and New York, 1972.) 158.40 DM : $50.30.

THIS is the fourth volume of a handsomely produced series covering several aspects of solar–terrestrial phenomena. It deals with ionospheric and magnetospheric problems and, as the editor K. Rawer points out in his introductory remarks, there is some overlap not only between the first two contributions but also with some articles published in earlier volumes. This was to some extent unavoidable. Again, there has been some delay, as much as 5 years, in the publication of these articles ; in a rapidly advancing subject such as this, this may be said to be a serious drawback. It by no means detracts, however, from the considerable and valuable accounts given of ionospheric and magnetospheric phenomena.

I found the first article, by Dr H. Poeverlein, on the Earth's magnetosphere particularly rewarding. There is a good and novel account of magnetodynamic theory. A section on fast

particles trapped in the geomagnetic field naturally includes some account of the radiation belts around the Earth, and discusses such problems as the source and loss of particles, their collisions and diffusion and the acceleration of trapped particles in which Alfven's mechanism, proposed originally in a theory of magnetic storms in 1939, is cited as an example. Convective motions in the magnetosphere, the solar wind and consequential terrestrial phenomena associated with the interaction of the wind with the geomagnetic field are included—for completeness, I think—and aurorae are also discussed at some length. There is a short section, contributed by N. Fukushima, dealing with more recent work such as the polar cusps, some recent theoretical work on the geomagnetic tail and the strong coupling between magnetosphere and ionospheric currents.

Dr Hess's article on the Earth's radiation belts naturally begins with charged-particle motions in a magnetic field. The inner and outer radiation belts are discussed at considerable length and there is a valuable account of the artificial radiation belts created by exploding nuclear devices high up in the atmosphere (including the Argus— the planning for which was well under way before the discovery of the van Allen natural radiation belt—Starfish and the USSR experiments).

The general characteristics of the outer radiation belt protons, α-particles and electrons are fully discussed, as are also their time variations, dependence on solar activity—including magnetic storm effects — aurorae and their associated X-ray fluxes. The article ends with a brief description of the radiation belts of other planets.

Dr Selzer's long article on rapid geomagnetic variations gives detailed definitions and discusses the various techniques of observations. Dr Selzer also considers at length the classification and morphology of the variations and, since these pulsations are usually ascribed to magnetospheric phenomena in which wave propagation plays an important part, there is naturally a theoretical section on the interpretation of the pulsations. The article includes an atlas of 69 plates showing examples of different types of observed variations including sudden commencements of storms (SSC) and so-called "pearls" or pc-1, pi-1, etc.

Finally we have a masterly article on waves and resonances in magneto-active plasmas, written jointly by Drs V. L. Ginzburg and A. A. Ruhadze. This highly mathematical and exhaustive review of the subject deals with foundations of plasma theory, particle collisions in plasmas, waves in plasmas —including magneto-active plasmas— the stability problem and oscillations

and waves in inhomogeneous plasmas. The approach is sometimes novel, as in dealing with the collision integral in a completely ionized gas, where the authors apply the methods of quantum mechanics rather than the classical method of collisions. In writing this article the authors have borne in mind the ultimate applications of the theory to the ionospheric and magnetospheric plasmas.

The present editors of the *Handbuch* are to be congratulated on the excellence of the volumes on geophysics which they have produced. Their inception, I believe, was due in large measure to the work and enthusiasm of the late Julius Bartels.

V. C. A. FERRARO

Noble Metals

Recent Advances in the Analytical Chemistry of the Noble Metals. By F. E. Beamish and J. C. Van Loon. Pp. xvi+511. (Pergamon: Oxford and New York, March 1972.) £14.

THIS book provides information on new techniques for the isolation and determination of the noble metals. It complements and updates the earlier excellent monograph in which Professor Beamish described the classical and some modern methods. It would be difficult to identify any significant publication on the analysis of noble metals which has not been referred to and received some critical examination in these monographs.

There are eight chapters covering methods of separation, atomic absorption, neutron activation, spectrochemical, X-ray fluorescence, electrometric, spectrophotometric, gravimetric and titrimetric procedures. Each chapter starts with an introduction which considers the techniques available and points out advantages and disadvantages. Frequently, areas where more research would be profitable, for example direct weighing precipitates for iridium, rhodium, platinum and ruthenium are identified. The authors also point out where much more research effort has been expended than is justified, for example spectrophotometric methods for palladium. For each element the alternative procedures are discussed and some suitable procedures selected for which practical details are given fully. Then follows a comprehensive review of published methods in which the authors' critical comments and identification of significant points are of considerable value.

The section on methods of separation includes ion exchange, precipitation, chromatography, solvent extraction and fire assay. The recently introduced technique of collection of noble metals in nickel sulphide could be usefully included in later editions.

The application of atomic absorption to noble metal analysis is satisfactorily covered and the twelve methods described in detail include applications to silver assay beads, geological materials and concentrates.

The information on neutron activation techniques is comprehensive and illustrates the wide applicability of these high sensitivity (sub p.p.b.) methods for any analyst having access to a suitable reactor.

The chapter on spectrochemical methods includes applications to rocks, ores, base metals and other noble metals. Particular attention is paid to pre-concentration. Spark source mass spectroscopy receives only a brief reference. Although X-ray fluorescence analysis plays an important part in the control of refining processes, information published on its applications is not extensive and this is reflected in a short chapter (14 pages) on this technique in which only three rather specialized methods are detailed.

The spectrophotometric section with 120 pages and forty-two practical procedures is extensive and there are comprehensive literature references. The summary of information in the tables is particularly noteworthy. Electrometric methods include polarographic, coulometric, amperometric, potentiometric and gravimetric procedures. The chapters on gravimetric and titrimetric methods record few improvements over those reported in the previous monograph.

This book and Professor Beamish's previous monograph together constitute the most comprehensive collection of information available concerning the analysis of noble metals.

W. WESTWOOD

Indicators Unlimited

Indicators. Edited by Edmund Bishop. Pp. x+746. (Pergamon: Oxford and New York, December 1972.) £12.

IN view of the well known facts about elephants and their gestation period, it comes as no surprise to learn that some of the contributors to this book found their material needed updating by the time the last sections had come in. A further parallel with the elephant is that very little indeed seems to have been forgotten. One wonders, however, whether the editor should not rather have styled himself a literary midwife, since by his own admission the editing was minimal, which is a pity because a little assistance here and there would have clarified certain parts for the reader. That the contributions by the Hungarian authors read so well is a tribute to the linguistic prowess of the writers.

Most practising chemists will undoubtedly use the book as a source of information about the indicators themselves, and skip the sections on theory. Those who probe further, however, may find a few questions arising. For example, on page 19 we have ion combination reactions giving rise to sparingly soluble molecules, which seems rather contradictory in terms. The word "precipitimetric" on the next page seems rather undesirable, and is followed by "principal reagent indication" which turns out to mean that the titrant serves as its own indicator in some way or other. Only two examples are quoted, and Aberdonians would like to see Clark's soap solution mentioned. One class of self-indication that is omitted is the disappearance of a precipitate as a result of complexation (as in the cyanide titration of nickel). It seems curious that self-indicator systems are treated so cavalierly (one paragraph and half a table) when the theory of redox systems seems to be dealt with three times over.

The discussion of one-colour indicators appears to overlook the fact that if the transition is from the colourless to the coloured form, then the first appearance of perceptible colour is taken as indicating the end-point, and the point at which this appears is dependent on the concentration of the indicator. Discussion of transition intervals for complete development of the colour seems slightly irrelevant. On page 54 there is a curious omission of the titrant concentration in the second line. The discussion of Job plots (page 59) omits to mention that they are not satisfactory for measuring very low values of formation constants and that the extrapolations are affected at least as much by errors in measuring absorbance as by errors in mixing the solutions. Indicators for determining the Hammett function are dismissed in a few lines, and the work on complementary tristimulus colorimetry in not much more.

On page 22 we have a "term under the log" (something nasty in the woodshed?), the third sentence on page 24 has a misplaced comma which acts as a full stop for the reader, and lower on the same page an indicator is busy converting logarithms to base 10. Page 31 says that curves were drawn on a computer, which is all that some people think computers are fit for.

Closer attention to proofreading might have avoided the mis-spelling of the name of one of the general editors, the address of the first contributor, and Volhard, and the introduction of a Scotch error on page 54. Sometimes there are different symbols for the same quantity, on the same page, and different spellings for the same compound (for example lucigenin(e)). The sign $\rightleftarrows$ is used in one section instead of $\rightleftharpoons$ to indicate equilibrium.

These comments refer to minor blemishes on what, after all, is the most comprehensive work of its kind and one that will be pre-eminent in its field for a long time to come. They are made here lest the reader, overwhelmed by the massive compilation of information, imagines that a bishop must be as infallible as a pope.

R. A. CHALMERS

Wave Functions

Molecular Wave Functions and Properties: Tabulated from SCF Calculations in a Gaussian Basis Set. By Lawrence C. Snyder and Harold Basch. Pp. vii+431. (Wiley: New York and London, January 1973.) £6.65.

THIS book is a tabulation of the ground-state wave functions calculated by the two authors for some fifty-six different molecules, all built up from hydrogen and first-row atoms of the periodic table. The first forty-two pages are introductory and serve to explain the nature of the calculations set out in the remaining 400 pages of text. These calculations cover molecules ranging from the hypothetical borane BH_3 with eight electrons to the forty-eight electron molecule C_2F_4. Only six of them are diatomic molecules—a very proper situation, since there would be little to say in favour of duplicating the existing tables of McLean and Yoshimine dealing with small linear molecules.

The simplest way to describe the contents of the book is to say, first, what numerical magnitudes are tabulated and, second, how they were obtained. Each molecule is represented by a table of up to eight pages. These pages begin with the molecular geometry (group symmetry and Cartesian coordinates of the nuclei, normally taken to be at the positions found by experiment); next comes an account of the various symmetries of the MOs, and a set of total energies (for example, total potential energy, total kinetic energy, total electron-electron energy, and so on). This leads to tabulated electronic moments of the final charge distribution taken up to fourth order. Then come a variety of other expectation values, such as powers of r, measured from individual nuclei) and the various quadrupole coupling terms. Mulliken charges and overlap populations lead to a summary of the coefficients that come in the LCAO forms of the MOs, a..d a final table of overlaps.

A strong point of the collection is that one set of atomic functions has been used throughout so that comparisons between different molecules is both straightforward and justifiable. Almost all the tables were printed photographically from a computer output so that few, if any, errors are likely to remain.

The calculations all lie within the framework of the single-determinant MO-method. As is usual nowadays each MO is expressed in LCAO form, and the expansion coefficients are found by the standard Roothaan technique. The component atomic orbitals have radial factors which are the sum of two parts, analogous to the double-ζ form using Slater orbitals. Here each part is a standard combination (or contraction) of two, or four, Gaussian functions, obtained as "best-atom" functions and incorporated into the POLYATOM program which was used. This leads to a total molecular energy about 0.05 a.u. per atom above the Hartree-Fock value. For many purposes this accuracy is sufficient: to improve on it would require configuration interaction and the numerical values of the inaccessible two-electron molecular integrals.

It is difficult to see just how important tables of this kind will become. Larger research centres will frequently have their own means for direct calculation; moreover there are many thousands of molecules which might claim a right to inclusion in a compendium of this sort and, lacking any possible incorporation of configuration interaction, it can say relatively little about excited molecular states. But this volume will prove useful and—in an age of economy—it is a good deal cheaper to buy it than use the program on which the results are based.

C. A. COULSON

Dynamics

Dynamic Behaviour of Processes. By John C. Friedly. Pp. xv + 590. (Prentice Hall: Englewood Cliffs, 1972.)

DYNAMICS is an essential part of most engineering disciplines, but the corresponding component in chemical engineering, process dynamics, has never quite been regarded as an entity of its own. This is almost certainly due to the dominance of steady-state operation in most physical and chemical processes. Accordingly, the study of process dynamics has been linked to that of process control, with far greater emphasis, in general, on the latter. In this book, Friedly has attempted to show that process dynamics has a place of its own in areas other than process control. I believe he has presented his case extremely well.

The greatest contribution of the book is a consistent, uniform, treatment of a wide range of dynamic problems with examples taken from a cross-section of recent chemical engineering literature. In each example the previously derived matrix equations are fully expanded, thereby illustrating the application of the relevant theory clearly and without

Ferrybridge Power Station

The day the cooling towers blew down at Ferrybridge C power station, Yorkshire (November 1, 1965). An illustration from *Britain's Weather, Its Workings, Lore and Forecasting* by David Bowen (David & Charles, £3.25), a non-specialist account which includes a description of the work of the Meteorological Office, and some hints on how to do your own forecasting if the Met. Office leaves you dissatisfied.

ambiguity. While the development of the theory is complete and self-contained, here again the emphasis is placed primarily on applications rather than on mathematical rigour.

After several introductory chapters on typical models and mathematical techniques, the book is divided into two (roughly) parallel sections on lumped and distributed parameter systems, dealing with linear and non-linear examples of both. The structure of partial differential equations is discussed in considerable detail, including illustrations of how the characteristics of the equations affect the dynamic behaviour of the corresponding systems.
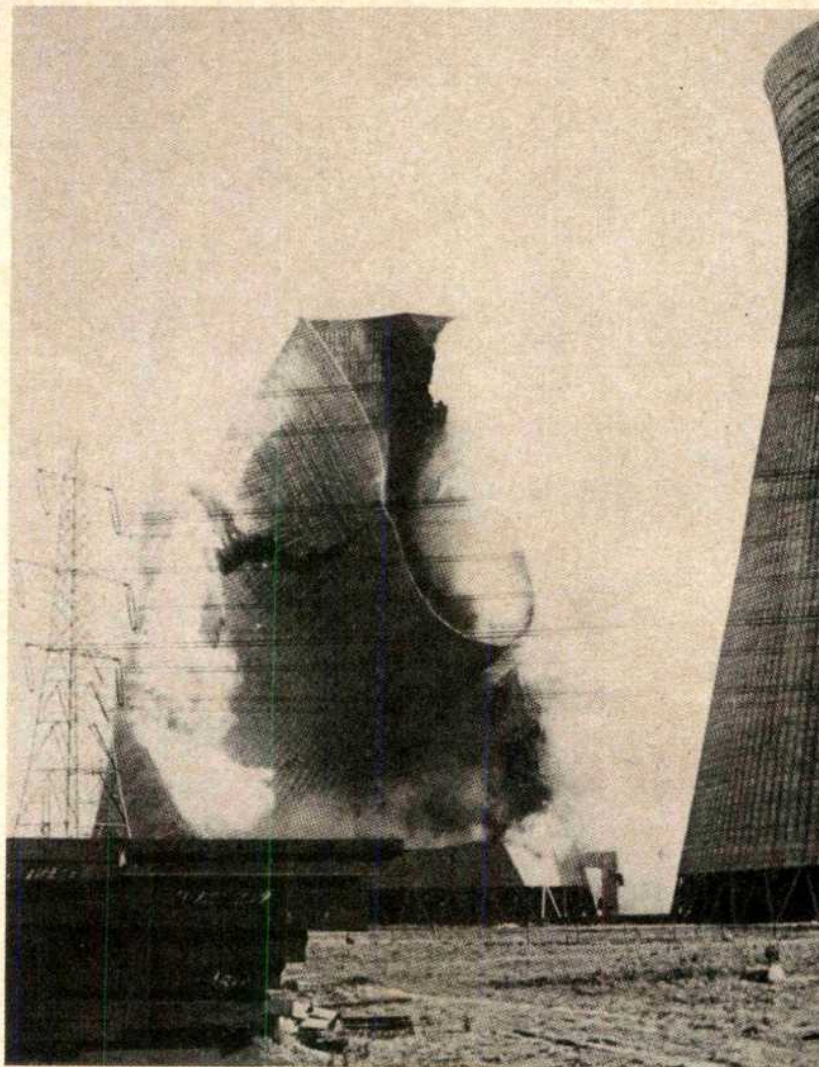
Several chapters are devoted to state space representation of dynamic problems. On these occasions the author has taken great care to point out the

relationship between modern state space representation and the conventional input-output (Laplace transform) approach. This should prove extremely valuable to students with a prior knowledge of elementary classical control theory.

The one drawback I can see with the author's approach is that, necessarily, several applications in the area of process control are not carried to their ultimate ends. This is especially true with optimal control, the subject which stimulated the growth of much of the theory discussed in the book. By attempting to stand process dynamics on its own, it was perhaps inevitable that the crutch of control theory be cast off, but a more complete picture might have been obtained otherwise.

L. KERSHENBAUM

Chemical Kinetics

Chemical Kinetics. Edited by J. C. Polanyi. Consulting Editor A. D. Buckingham. Pp. 322. (MTP International Review of Science. Physical Chemistry. Series one, Volume 9.) Pp. 322. (Butterworth: London; University Park: Baltimore, Maryland, 1972.) £10.00; $24.50.

TWENTY-TWO years ago, volume 1 of *Annual Review of Physical Chemistry* was inaugurated with an ambitious survey, including eighteen sections, one of which, *Chemical Kinetics,* gave a reasonable coverage of that then relatively young field. It is a reflexion of our time that Butterworth has now announced a new series to review biennially all of chemistry in 33 volumes and three indices. Volume 9, *Kinetics* is one of thirteen volumes of the series devoted to physical and analytical chemistry. It contains ten chapters by very well-known research workers under the categories of reactions: unimolecular, by D. W. Setser, including for the first time that of ions; bimolecular, by I. M. Campbell and D. L. Baulch, mostly of atoms and small radicals; free radicals, by E. Whittle; hot atoms, by F. S. Rowland; chemiluminescence, by T. Carrington and J. C. Polanyi; molecular beams, by J. L. Kinsey; ion-molecules, by J. Dubrin and M. J. Henchman; solvated electrons, by F. Dainton; energy transfer, by J. I. Steinfeld; and relaxation techniques, by J. E. Crooks.

The material covered extends, in general, from 1967 to 1971 though many of the authors have chosen to avoid overlap with recent reviews, and so cover only the period 1970–1971. The second set of thirty-three volumes will cover the period 1972–1973 and is scheduled for 1974. The style is that of the typical review and does not lend itself to easy reading, except by specialists. The reviewers in general, however, write well and with authority so that the volume is excellent for conveying to the "cultured" scientist current progress in each field and some flavour of the directions and interests of kineticists today. Its greatest usefulness, however, will be to the research worker and specialist for whom it will represent an appreciable saving in time. In spite of its length, it suffers from the fault of most reviews of being descriptive rather than critical, so that apparent or hidden contradictions are not resolved. This is possibly the inevitable state of any active research field. There are a relatively few, but glaring typographical errors.

In these days of shrinking library budgets and expanding scientific literature (both original and review), the author refrains from judgments on the transient or ultimate utility of so imposing and expensive a project. At about £10 ($24.00) per volume, it will represent a forbidding investment in money and space to both libraries and research workers. Perhaps this only underlines one of the most painful and critical weaknesses of science today—our archaic communications system.

S. W. BENSON

Statistics of Spectra

Gamma-ray Spectroscopy, with Particular Reference to Detector and Computer Evaluation Techniques. By P. Quittner. Pp. 111. (Adam Hilger: London, 1972.) £4.

THERE have been two revolutions in the field of gamma-ray spectroscopy since 1946. The first came in the late forties with the advent of the scintillation counter. This provided the first efficient gamma-ray detector as well as a spectrometer of rather poor pulse height resolution.

The emergence of the Ge(Li) semiconductor detector in the early sixties produced the second revolution. With this detector, the high counting efficiency attained with the scintillation counter could now be complemented with a superb pulse height resolution which, in many cases, can surpass the best resolutions obtainable with magnetic and crystal spectrometers.

This little book is not primarily concerned with the physics of these counters, but rather with the many elaborate statistical techniques that have been devised as aids in the interpretation of their spectra. As such, it has been written very much for the specialist and does not make light reading.

Its main part surveys techniques of spectrum smoothing, detector response function, peak location, peak area determination, weighted least squares resolution and spectrum stripping. Another chapter is devoted to miscellaneous applications such as decay curve analysis programs, detection limits and on-line applications.

The value of these surveys lies not so much in their aiding the implementation of the techniques, but rather in a discussion of their scope, supplemented with a lengthy list of references. One shortcoming is the fact that, although these techniques rely implicitly on computers for their execution, very little mention is made of the many programs that are now accessible to all workers; but maybe this is too much to expect from a work of this size.

This book can be expected to play an important role in the future for workers in the fields of nuclear and particle physics, activation analysis, X-rays, and more generally workers in many other fields involving statistical observations.

D. K. BUTT

Earth Science

Geophysical Surveys. Edited by Wm. Markowitz. (*An International Journal of Geophysics.*) Vol. 1. No. 1. Pp. 119. (D. Reidel: Dordrecht, September 1972.) $25.29; Dfl. 170 (libraries and institutions). $22.75; Dfl. 70 (individuals).

THE appearance of a new earth science journal is not nowadays such a rare event. Over the past few years a number of publications, each catering for a limited range of interest, have appeared, the great majority of them having their birth in publishing houses and not the learned societies.

The title "Geophysical Surveys" means "exploration" to most earth scientists, and "Geophysical Reviews" might better describe the contents of the first issue and indeed the aim of the journal as a whole. The object of the publication is to provide a contemporary synthesis of progress in various branches of "geophysical research". Each article is preceded by a full explanatory introduction to give background and aid in understanding the significance of the work.

This first issue contains papers on earthquake prediction, the Rhine Rift Valley, the hydraulics of the stream flow, tidal flow and the Earth's core. Papers are by invitation only and original research papers will not be included. The papers are indeed informative and there is certainly a crying need for papers of this kind—and not just in this branch of science—which collates a lot of information together in one place. It is almost impossible nowadays to keep abreast of all journals in earth science, in a particular field, and the thought of reading one journal, which updates progress from time to time, will doubtless appeal to many.

Even so, for this privilege institutions are asked to pay about £23 a year, whilst individuals receive the quarterly issues at about £9.50 which at nearly £2.40 an issue borders on the expensive. Would-be readers will have to decide if the convenience of these reviews justifies the price. J. R. V. BROOKS

Pulp and Polymerization

Chemical Modification of Papermaking Fibres. By Kyle Ward, jun. Pp. viii + 246. (Marcel Dekker: New York, December 1972.) $18.50.

THE orthodox maker and user of paper tends to treat his fibre as an inert material and to forget that cellulose is both a polymer and an alcohol and therefore capable of entering into many interesting and possibly useful chemical combinations. The chemist who wishes to study more thoroughly the reactions

which cellulose may undergo has to wade through masses of literature primarily concerned with either textiles or polymers. This may be tedious and can be annoying. One can find large books on these subjects in which "paper" appears rarely in the index and one can even find tabulated data on cellulose fibres in which wood pulp, in terms of tonnage the most important of all, is not mentioned.

The book by Emeritus Professor Kyle Ward fills a necessary gap. It will do much to encourage the reader primarily interested in the chemical properties of pulp and paper fibres. The reactions of pulp and paper fibres are grouped in chapters on esterification, etherification, oxidation, cross linking and graft polymerization. Nearly all the references are directly concerned with pulp and paper and in each chapter the author discusses possible uses of the reactions described. Many of the references (there are over 800) are to patents, frequently taken out by chemical manufacturers.

Cross linking has been used for over thirty years in making "wet strength" papers but the cross linking references are all in one chapter and this is helpful to the theorist. Alkyl ketene dimers have now been sold for sizing for eighteen years but we find them in the same chapter, on esterification, as the older processes for partial acetylation of paper for dielectrics. The grouping of reactions according to their chemistry is refreshing—in most books on paper making they would be grouped according to their part in the process.

These are important differences between pulps due to the effects of side chains. Paper made from pulp with hydrophobe side chains is weak, unless made from a non-aqueous solvent, but paper already made can be chemically modified without loss of strength.

We should be grateful that Professor Ward has found the time and energy to write this book. He has made good use of the unrivalled library facilities at the Institute of Paper Chemistry, Appleton, Wisconsin, for the benefit of all of us.

F. LYTH HUDSON

Physical Geography

Environmental Geomorphology and Landscape Conservation. Edited by D. R. Coates. Volume I: Prior to 1900. Pp. x+485. (Dowden, Hutchinson and Ross: Stroudsburg, Pennsylvania, January 1973.) £9.75.

THIS is the first of three volumes concerned with man's use of his physical environment, forming part of a "Benchmark Series" of geological texts. The aim of the series is to ease the availability of many important papers by reproducing them in a facsimile fashion along with sectional editorial comments.

In this particular volume, variation in the quality of reproduction is a reflexion of the original material but the photographs have not generally reproduced well. The book would be far easier to read had all the papers and diagrams been re-set and re-drawn. Professor Coates has collected together thirty-three diverse publications on the theme of man's exploitation of his environment before 1900.

The text is subdivided into five sections: the first illustrates the importance of water to man. The next contains articles by Barnes and Semple—both showing the influence of terrain on man. It is a pity that these publications on geographical philosophy represent solely the deterministic outlook. The third section contains a variety of descriptions of the United States from the early eighteenth century to the rather interesting First Annual Report of the United States Geological Survey in 1880. The effect of man on the physical environment is well illustrated in the fourth section, with articles on such topics as the reasons for the decline of the Roman, Mayan and ancient Mesopotamian civilizations. It is most fitting that this section is concluded by a paper by G. K. Gilbert who, in examining the effect of sediment production from hydraulic mining, raised many environmental themes of marked relevance today. The final section on landscape conservation includes two papers on ancient agriculture in the Negev desert which have relevance to present day agriculture in that area. Other papers in this section are representative of early writings on the need for conservation techniques in agriculture. A short extract of Sir John Sinclair's writings is included; it tends to be forgotten in Britain today that the need for soil conservation measures has been stressed since the early days of the agricultural revolution.

The only general criticism which can be made of the book is its title: many of the papers cannot be termed truly geomorphological; and geomorphology must, by definition, be environmental. Instead the book is a collection of essays on physical geography and some other title ought to have been devised. The title, however, is of little importance compared with the contents. The two principal contributions of this book are to present in one volume many diverse publications and, more importantly, to add a great deal of perspective to present day environmental debates. This is achieved by showing that man from very early times has greatly modified his environment, often consciously, and hence some of the consequences of present day exploitation ought to be assessed by reference to past events.

DONALD A. DAVIDSON

Microwave Ultrasonics

Microwave Ultrasonics in Solid State Physics. By J. W. W. Tucker and V. W. Rampton. Pp. x+418. (North-Holland: Amsterdam, 1972.) Dfl. 130; $40.75.

SOME justification is needed for a volume on ultrasonics that deals only with frequencies above the apparently arbitrary limit of 1 GHz. The explanation is that 1 GHz was the maximum frequency that could be achieved by the traditional method of ultrasonic generation using a resonant piezoelectric transducer. Recently, techniques have become available for obtaining frequencies much higher than this figure, as high as 114 GHz in one experiment, but more typically in the range 3 to 10 GHz. The authors of the present book state that it has been their intention to concentrate on the areas of solid state physics that have become ultrasonically accessible only as a result of these advances. In this aim they have generally been successful, although their choice of material does sometimes appear a little arbitrary and incomplete.

The book begins with two short chapters embodying a brief historical development of the field of microwave ultrasonics and a short theoretical survey of elastic wave propagation in solids. An experimental chapter describes in detail the techniques that are used for generating and detecting ultrasound at microwave frequencies. Particular emphasis is given to non-resonant piezoelectric, magnetostrictive, and thin film transducers. Satisfying experimental detail is provided on such aspects as the design of microwave cavities, the preparation of specimens, and the evaporation of piezoelectric films.

Chapter 4 deals with the attenuation of ultrasound in dielectric crystals, that is, by scattering from thermal phonons. The topic is lucidly developed, and the importance of key features such as elastic anisotropy and thermal phonon lifetime is carefully explained. This is followed by one of the more controversial chapters, on the propagation of ultrasonic waves in ferromagnetic materials. There are two criticisms to be made of this section. Roughly half the chapter, about twenty pages, is devoted to an unnecessary review of the spin wave theory of ferromagnetism. Furthermore, most magnetoelastic experiments have been carried out at frequencies below 1 GHz and it is not clear that microwave ultrasonic studies have contributed greatly to the subject.

The converse is true of acoustic paramagnetic resonance, a field the development of which has been made possible only as a result of the advances in microwave ultrasonics, and also one

with which the authors have been closely associated. For this reason, perhaps, the chapter is particularly comprehensively written, with details not only of relevant crystal field theory and the spin-lattice interaction, but also of such relatively esoteric topics as rotatory dispersion and the phonon maser.

The amplification of ultrasound that can take place in some semiconductors is also treated in detail, with a useful discussion of non-linear and acoustoelectric effects. Metals are mentioned only very briefly, on the questionable grounds that this is a low frequency topic. Mechanisms of ultrasonic attenuation by electrons are summarized and referenced, including those present in superconductors. The final chapter reviews the interaction of light with microwave ultrasound as studied by the techniques of Brillouin and stimulated Brillouin scattering. There are several useful appendices, mainly of crystal matrices and coefficients. Inevitably, certain sections of the book are already out of date, and the references are complete only up to 1970.

The book has been written at the first or second year graduate level and the mathematical formalism is presented in a clear and helpful manner. It is perhaps fashionable to criticize the price of books; nevertheless the figure of £17 cannot be allowed to pass without comment, because it is likely that those for whom the book is intended will not be able to afford it.

J. K. WIGMORE

Non-magnetic Metals

Introduction to the Theory of Normal Metals. By A. A. Abrikosov. Translated by Alex Baratoff. Pp. xi + 293. (Academic: New York and London, 1972.)

As is apparent from the title, unlike other supplements to *Solid State Physics*[1], this is not a scholarly treatise on a specialist topic. Rather, it is a very unusual introductory text to the theory of non-magnetic and non-superconducting metals. Roughly speaking, it consists of a rapid sequence of "order of magnitude" calculations pertaining to the physics of normal metals.

Conventional topics like energy bands, Fermi liquid theory and scattering processes which give rise to resistance are quickly disposed of in the first four chapters. The rest of the book, ten more chapters, is devoted to problems which only recently have been explored in any detail. Many of these, like the various size effects, helicon waves, magneto plasma waves and Fermi liquid effects, are not yet part of standard texts on metal physics.

The calculations are short—the discussion is kept to a minimum—they are frequently novel, and always instructive. Using only the most elementary means, Schrödinger's equation, Boltzmann equation, and so on, the author contrives to make first principle calculations of such complicated effects as the giant oscillations in ultrasonic attenuation and the like, always including sufficient detail to enable the reader to follow each mathematical step. At the end of each calculation numerical estimates are given of the absolute magnitude of the effect.

There is no attempt at rigour. The aim is always to isolate the main contribution and to exhibit why the effect is interesting from the point of view of the basic interactions. On this level the book is an intellectual *tour de force*.

As the author warns the reader in the preface, the topics covered reflect his research interests. These are largely that of a many-body theorist and show up to an adverse effect in the rather misleading summary of the current state of band theory in chapter 14.

Nevertheless, it should make an interesting and an edifying reading for any solid state physicist, experimentalists and theorists alike. It should also be useful as a text in a more specialized course on metal physics for postgraduate students or as an outside reading for honours students doing solid state physics.   B. L. GYORFFY

[1] Ehrenreich, H., Seitz, F., and Turnbull, D. (eds), *Solid State Physics* (Academic Press: New York and London).

Angle on Aromaticity

The Aromatic Sextet. By Eric Clar. Pp. x + 128. (John Wiley: London and New York, December 1972.) £1.50.

THREE groups of people should buy a copy of this book. Anyone who works with polynuclear systems will find in its pages an astonishing amount of factual detail; any theoretical chemist interested in electronic spectra or aromatic molecules should buy a copy and find a life's work of unsolved problems; anyone who knows Clar, or who has ever worked with him, will find here the familiar uncompromising interpretations of the experimental results which he has so indefatigably compiled.

Yet there will be few undergraduate courses that will adopt it, because so much of the theory in it offends against the accepted framework of bonding and aromaticity which all chemists (except Clar) subscribe to. Is he a latter-day Copernicus, and are we all wrong?

Clar considers the familiar circle inside the formula for benzene as an almost inseparable set of six electrons—Robinson's aromatic sextet. In naphthalene therefore only one ring at a time can be truly benzenoid (containing a sextet)—the other ring only possesses four π electrons! Anthracene likewise can only have one ring benzenoid at a time, whereas phenanthrene can have two benzenoid rings, leaving the 9,10 bridge with a localized double bond.

Clar goes on to treat more complex hydrocarbons in the same rigorous way, counting the number of rings which can simultaneously contain the magical aromatic sextet. When this is done, he can offer rationalizations of bond localization, chemical shift values, coupling constants, reactivity, and electronic spectra. These empirical computations might be christened "Clar's rules" to take their place with the Woodward rules of ultraviolet, or the Shoolery rules of nuclear magnetic resonance spectra.

What is needed for the moderates among us is a companion volume written from the standpoint of theoretical orthodoxy—but which is equally successful in explaining the facts. To my knowledge this will be a long time in coming.   WILLIAM KEMP

Ostracods in Stereo
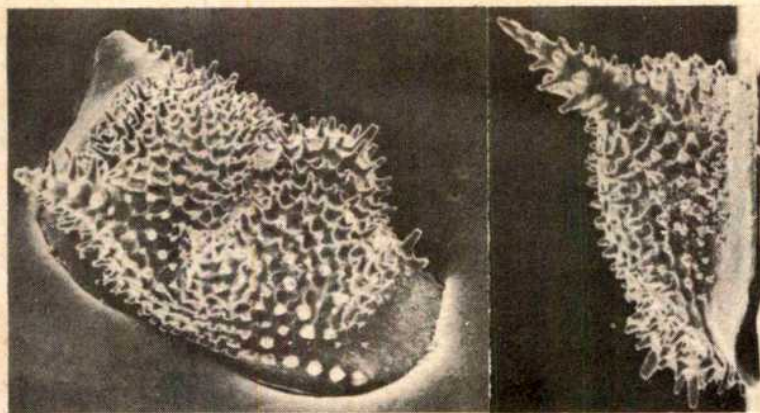
Ostracod shells from *A Stereo-Atlas of Ostracod Shells,* by P. C. Sylvester-Bradley and David J. Siveter (Department of Geology, University of Leicester, 1973). The atlas is designed specifically to meet the needs of palaeontography, in which the study of fossils is strictly descriptive rather than interpretative.

Biological Sciences

Circulatory History

The Heart and the Vascular System in Ancient Greek Medicine: From Alemaeon to Galen. By C. R. S. Harris. Pp. ix+474. (Clarendon: Oxford; Oxford University: London, February 1973.) £15.

HARVEY's discovery of the circulation of the blood (1628) was not made in a vacuum. It truly was a Copernican revolution. As such it provided a completely new vision against a *corpus* of time-honoured observations and interpretations. This had essentially not changed since having received its final form and codification by Galen in the second century AD. Indeed it was a formidable array of shrewd observations mostly anatomical and even experimental, and of theories as well as perfectly rational and methodical argumentation. It had seemed to serve well physiology, medicine and natural philosophy. New anatomical discoveries in the Renaissance, however important, had remained on the level of detail and failed to bring about the crucial breakaway from the Galenic view. In this view the origin and motion of the blood had been decentralized and the liver sent venous blood to the periphery in a way analogous to the production of arterial blood by the heart. And there the matter rested. *Ex post facto* we may wonder why the ancients and their millenary successors did not arrive at the correct view. Before doing so, however, we require exact knowledge as to how far they had advanced in reality. In spite of the voluminous literature concerning Harvey and his predecessors no such comprehensive critical and detailed account has been available and wild claims on behalf of Galen have been allowed to pass. This unsatisfactory situation has now happily changed through the truly illustrious work under notice. Based on hundreds of *loci* (translated and given in the full original in the footnotes) the merits and failures of the ancients (and this implies of many an author up to Harvey) are critically weighed and presented in a crisp and clear style enlivened by delightfully humorous asides. Two outstanding parts of the narrative deserve special mention: Aristotle's three "ventricle" theory of the heart and Galen's finds and ideas concerning the pulmonary transit of blood. Why Aristotle should have assumed the heart to consist of three "ventricles" was explained elegantly and convincingly by T. H. Huxley (1880) and more recently by Erich Mühsam (1910) in observational terms. Both concluded that the whole of the right heart should have impressed

Galen as one, the left ventricle as the second ("middle") and the left auricle as the "third" cavity of the heart. For this observational interpretation the reviewer calls to witness no lesser Aristotelians than Harvey himself and Conring. Nevertheless the author finds contradictions and inconsistencies when all *loci* are taken into account. He would rather see in Aristotle's thesis the expression of his pre-occupation with "the mean" (*mesotes*)—a principle paramount in Peripatetic natural philosophy. Phenomena were then reduced to the interaction of opposites (*enantia*) possessed of a common "mean". It seems to me that the objections, though unanswerable in detail, neither detract from the interpretative value of the anatomical explanation nor make the latter incompatible with the metaphysical argument so aptly adduced by the author. Both would seem to entitle Aristotle to what may impress us as an advance rather than "error" when duly interpreted in context. No doubt can any longer remain of Galen's ignorance of the (misnamed) "lesser circulation". He was aware of the intra-pulmonary transit of venous blood into the arterial channels, but made no provision for its further progress into the left auricle. This admitted air alone and that for cooling and not for heating. Nor is there room for any "solution" of air in blood. With the clear demonstration of the bare facts culled from all the twenty odd volumes of the standard edition of Galen (Kühn) the wasps' nest of modernizing misconceptions and almost juridical and misleading pleas on Galen's supposed anticipation of Harvey and his immediate anatomical predecessors has been swept away. Indeed Galen was a conservative and never had any idea of blood circulation —neither of the so-called "lesser" nor of the "greater"—systemic—circulation. The reasons here given are: (1) the misconceived nature of the pulse and its connexion with the movements of the heart; (2) the view of the heart as centre of the respiratory system; and (3) the appraisal of the blood as a nourishment that was continually consumed in the periphery. In spite of his advanced anatomical knowledge, his insight into the propulsion of blood into the lungs as well as into the arterial system and the connexion of arterial and venous channels through capillaries he failed to notice the venous valves—a structure which assumed first-class dignity in Harvey's *inventio*. It should not be forgotten, however, that in some points of detail Galen had held more correct views than Harvey—the latter's disregard of the differences between the

arterial and venous blood, as emphasized by Galen, his adherence to the Aristotelian principle of the singleness (*henotes*) of the blood was a *felix culpa* which not unlikely promoted his discovery. Nor was Galen's belief in active "attractive" powers of diastole of the right atrium as wrong as Harvey thought. And finally we should not forget ideological reasons such as again the Aristotelian monocentricity of the blood as located in the heart (in contrast to its Galenic decentralization) which must have impressed Harvey, the staunch Aristotelian. Above all and overriding there was Harvey's quantification—it provided the initial "hunch" for the discovery which started as an idea and challenge to be proved by empirical evidence at this stage still wanting.

Here, then, we have a definitive work through which misleading seals and obscurities have been removed in a field of perennial significance for the historian, the physiologist and biological scientist at large. It is not a "bedside" book, to say the least, but a classic calling for careful and detailed study. It will amply reward its perusers in all future.

WALTER PAGEL

"Seeing" with Skin

Brain Mechanisms in Sensory Substitution. By Paul Bach-y-Rita. Pp. xiv+182. (Academic: New York and London, September 1972.) $9.75.

THE first chapter of this book and parts of the second describe the equipment designed by Dr Bach-y-Rita and his colleagues for the conversion of optical images into patterned vibratory or electrical stimuli that can be applied to the skin. Part of the fourth chapter and a small part of the sixth describe results obtained with the equipment, chiefly on highly trained blind subjects.

The remaining two-thirds of the book is a review of some topics in sensory neurophysiology. This review is accurate, and contains some small original ideas; but there is very little connexion between it and the sensory substitution part. I was unable to find a single conclusion about brain mechanisms drawn by Dr Bach-y-Rita from his observations on sensory substitution; nor was I able to draw any myself. I could find only very few places in the book where facts discovered by physiological methods are used in interpreting the observations on sensory substitution, and in these few places the facts cited are well known and their application obvious; if the interpretative remarks had been omitted, they

could have been supplied by almost any reader.

The real importance of Dr Bach-y-Rita's work is not in the elucidation of brain mechanisms, to which it has not yet contributed anything and does not look very likely to contribute anything in the future. The field in which the work clearly may, if it succeeds, be immensely important is that of helping blind people. In this field, I think the ultimate criterion of success is clear: an invention has succeeded only if many blind people procure it at cost to themselves in money or inconvenience and then persist in using it as part of their everyday living. Dr Bach-y-Rita does not seem to claim to have met this criterion yet, but he would probably accept it as the right ultimate one. Where he and I probably differ is on criteria for partial success. I think a device has achieved significant partial success only when it has enabled a blind person to perform, better than he could without the device, an objectively assessable task of a kind that many blind people want to perform. Reading ordinary print or handwriting is such a task. A device for converting letters into auditory signals, the 'Optophone' of E. F. d'Albe, allowed a trained blind person to read ordinary print as early as 1917, but never met the ultimate criterion of success because reading by the auditory signals was slow, and learning to do it was very difficult. The 'Optacon' of Linvill and Bliss, which converts letters into tactile signals read with the fingers, allows faster reading with less preliminary training, and has nearly (perhaps quite) reached the ultimate criterion of success. Another objectively assessable task is to avoid obstacles, including moving ones, in walking. Any new device for this purpose has a formidable competitor in the guide dog.

Dr Bach-y-Rita concerns himself very little with the performance of his subjects in such objectively assessable tasks. There is one sentence on the reading of letters on page 90 which indicates a performance about ten times slower with his equipment than is commonly achieved with the 'Optacon', and a qualitative remark about the reading of graphs on page 152; beyond these I can find nothing. The attitude of the present book is well expressed in a sentence on page 156: "The theoretical basis for the design of the vision substitution system described above implies a concept of a brain so malleable that the subjective experience of 'vision' (as well as the quantitative and qualitative afferent information necessary for useful 'vision') could be obtained through an artificial receptor projecting to the cutaneous receptors".

Many blind people have vivid visual imagination, and describe themselves as "seeing" things that they feel with their hands or with a stick. I shall be surprised if different visual substitution systems that are similar in the amount of information they convey prove to differ much from each other in the capacity for evoking such "seeing". The relative merits of any two proposed systems will be best measured by their capacity for conveying useful information in a non-technical sense; but information in the strict mathematical sense will surely be better than anything so intangible as whether the patient describes himself as seeing.

Devices that stimulate central parts of the visual pathway have a different status in this respect. We know from observations on sighted subjects that the sensation that they produce does not merely somewhat resemble vision; it is absolutely indistinguishable from it. Yet even here the important consideration is not the kind of sensation, but the efficiency with which it conveys useful information. In this respect, implanted stimulators of the visual cortex have not yet done as well even as Dr Bach-y-Rita's apparatus, and the 'Optacon' at present altogether outclasses them.

G. S. BRINDLEY

Developmental Metabolism

Critical Variables in Differentiation. By B. E. Wright. Pp. 109. (Prentice Hall: Englewood Cliffs, New Jersey and Hemel Hempstead, 1973.) £4.

THIS is both an interesting and a disappointing book. Its theme is that most developmental biologists are pursuing the wrong goals. Instead of looking at gene activation and rates of enzyme synthesis during development they should concentrate on the role of substrates and products and the control of metabolism by their complex interplay. This theme the author states forcibly and well. The book is disappointing, however, when it comes to the evidence.

The book falls into four parts, beginning with a review of selected data in the literature that confirm the author's contention that observed changes in enzymic activities in differentiating tissues need not be "critical variables" on which the rate or course of development depends. The second section starts with a description of carbohydrate metabolism during differentiation in the cellular slime mould *Dictyostelium discoideum*. The author reviews the enzymes that have been studied in this organism by various workers and then taking them one by one attempts to discredit their role as critical variables in development. The third section then presents a model of the metabolism of carbohydrate in *Dictyostelium* that is sufficiently simplified to be programmed into a computer using a specialized

"metasim" program. The computer duly predicts that the critical variables in nearly every case are not the enzymes that people have investigated but their substrates or products. The last section is concerned with speculation about the evolution of closed developmental systems. This section seems to be out of place in this book and will not be further discussed.

The book is generally well written and the arguments are lucidly presented. The diagrams are clear and helpful with the notable exception of Fig. 5, which is so involved that it looks as if it is intended to be a mental maze.

My main criticism concerns the use of the simplified metabolic model coupled to a computer program, which seems to lead to unwarranted conclusions based on numerous questionable assumptions. For example, on page 86 it is concluded that "in the case of UDPglucose pyrophosphorylase, although the enzyme activity and reaction rate increase together during differentiation, the increased enzyme level is not a primary critical variable—that is, it is not directly responsible for the enhanced reaction rate". The evidence for this comes from a computer analysis of a model of metabolism (page 58) that supposes that glycogen synthesis and degradation are in a closed cycle which is at steady state equilibrium at the start of development. Of the rate constants for the three reactions, (1) the synthesis of glycogen from UDPglucose, (2) the breakdown of glycogen to glucose-1-phosphate and (3) the synthesis of UDPglucose from glucose-1-phosphate, only the latter is known. The others were "found by assuming that at aggregation no end-product saccharides are synthesized and that a steady state exists; that is, the rate of UDPglucose synthesis equals the rate of soluble glycogen synthesis equals the rate of glucose-1-phosphate production". With these assumptions the author then demonstrates with the aid of a computer that increasing the activity of the enzyme UDPglucose pyrophosphorylase, which catalyses the third reaction above, does not increase the amount of UDPglucose formed but merely reduces the already small steady-state level of glucose-1-phosphate still further (page 61). This result is inevitable, however, because of the assumption made in the model of a fixed rate of glucose-1-phosphate production from glycogen. If glucose-1-phosphate is not made to be limiting then the computer shows that more UDPglucose is formed without raising the activity of UDPglucose pyrophosphorylase, but nowhere does the author show the computer prediction of the case in which UDPglucose pyrophosphorylase activity is increased along with an increase in glycogen

breakdown to maintain the levels of glucose-1-phosphate at those the author actually observes *in vivo*. In such conditions the activity of UDPglucose pyrophosphorylase would clearly have been shown to control the extent of UDPglucose production.

This and other parts of the model also depend on the highly questionable assumption that none of the metabolites whose conceneration are calculated are at all compartmentalized (that is the amount of metabolite measured in the cell is divided by the total cell volume to get the concentration *in vivo*). The notion that compartmentalization can be allowed for by finding the effects of altering the substrate/Km ratio of a particular enzyme (page 64) seems also unsound particularly because the Km is altered rather than the substrate concentration.

This book is thought provoking and the principles expressed may well be very important, but the simplified metabolic models that are used are not worthy of the principles invoked.

PETER C. NEWELL

Environmental Physiology

Physiological Adaptations: Desert and Mountains. Edited by M. K. Yousef, S. M. Horvath and R. W. Bullard. Pp. xiv+258. (Academic: New York and London, September 1972.) $14.50.

Life, Heat and Altitude by D. B. Dill was published in 1938 and has continued to influence physiologists. Today, Dr Dill is actively working at the Desert Research Institute, Boulder City, Nevada, where a symposium was held in celebration of his eightieth birthday; this volume is a record of the proceedings. Many of the contributors were associated with Dill at the famous Harvard Fatigue Laboratory, and inevitably some papers emphasize experimental work in which they collaborated with Dill, but the volume is far more than a collection of physiological reminiscences or personal tributes. There are twenty-six chapters, with an impressive list of authors, all distinguished for work on environmental physiology. It is not possible to review each chapter; only a few aspects can be mentioned. E. F. Adolph, himself an active veteran of environmental physiology, has brought up to date his ideas on "general concepts of physiological adaptation", which he summarizes as "superfunction is an end product of physiological adaptation". R. A. McFarland, who was also a member of the Harvard Fatigue Laboratory, has restated his views on the role of oxygen in the process of ageing, revised in the light of recent work on the effects of altitude. H. S. Belding discusses the mechanisms of acclimatization to heat, and emphasizes the term "quickening" as exemplified by the more rapid onset of sweating in the acclimatized compared with the unacclimatized individual. A. P. Gagge writes on "Partitional Calorimetry". This is a really valuable contribution, not so much because of novelty as in the clarity and precision with which a difficult subject is presented.

L. D. Carlson, whose recent death has deprived us of one of the most thoughtful and penetrating workers in this field of physiology, in a "speculative analysis of certain aspects of adaptation", points out that desert animals are not exposed to a constantly hot environment but regularly encounter the heat of the day and the cold of the night. Furthermore, "many desert animals live in the mountains nearby as well" and hence may need to adapt to altitude as well as heat and cold. Carlson uses many of Adolph's concepts, rewording them as, for example, "A biological system is inconceivable without its external environment". He discusses "responses that may be time-dependent within the time range of day-to-day existence" and wonders if the difficulties of interpreting climatic factors in evolution may be due to the use of average climatic conditions, instead of examining the effects of a range of conditions.

D. H. K. Lee's chapter "Large Mammals in the Desert" draws extensively (and rightly) on the work of Schmidt-Nielsen and his colleagues, but he also draws on his own work on man. He makes the interesting point that upright man at noon presents a minimal area for solar radiation, as indeed others have shown, but in contrast a quadruped such as a cow receives about the same large radiant load virtually throughout the day. "Small Mammals in the Desert" by W. G. Bradley and M. K. Yousef, is concerned with the "complex interlocking patterns of behaviour and physiology" which make it possible for

Nocturnal Insectivores
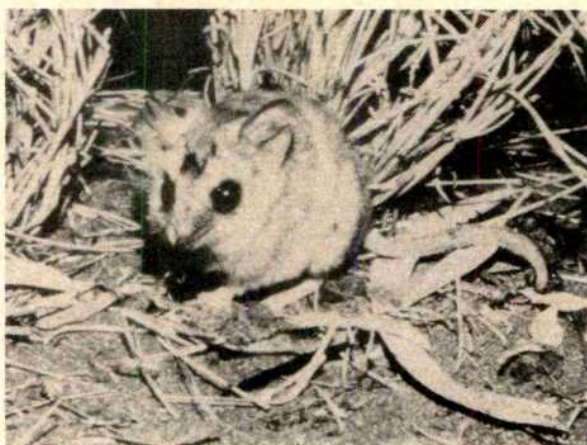
Dasycercus cristicauda (top) and *Sminthopsis crassicaudata* illustrate two different types of water economy found in desert animals sharing the same ecological niche. *D. cristicauda* has a low water turnover, *S. crassicaudata* a high one. The two animals are illustrated in the chapter by W. V. Macfarlane and B. Howard in *Comparative Physiology of Desert Animals,* edited by G. M. O. Maloiy (Academic Press, New York and London, 1972).

large numbers of small mammals to flourish in the desert conditions of temperature extremes, water scarcity and food shortages. The behavioural aspects of temperature regulation have been neglected by physiologists until recently; the desert animal provides opportunities for studying behaviour as a physiological component of a range of adaptation.

Articles by W. H. Forbes, B. Balke, R. W. Bullard, C. F. Conzolazio and S. M. Horvath deal with various aspects of adaptation to altitude. Although in most of the book there are few reports of new work, the individual writers have taken the opportunity to have a new look. The results are varied but are stimulating because of a number of unexpected and exciting ideas.

O. G. EDHOLM

Adaptation in the Sea

Environmental Physiology of Marine Animals. By Wiona B. Vernberg and F. John Vernberg. Pp. ix+346. (Springer: New York and Berlin, 1972.) 62.40 DM; $19.80.

THE purpose in writing this book was to bring together in a text for college and graduate students the main concepts encountered in the physiology of the marine environment. The result is a concise, readable attempt to describe the functional responses of marine animals to alterations in the environment. The first chapter is concerned with definitions related to the functional processes in organisms, to detection by the organism of changes in its environment and to the physiology of adaptation. Some interesting aspects of the duration of exposure to stressful environmental factors are mentioned briefly. There follows a condensed account of the characteristics, chemistry and physical properties of sea water which also gives definitions involving the relations of organisms to temperature, pressure, tides, salinity, light and other factors. The marine environment is considered subsequently in four main sections: on the intertidal zone, the estuarine environment, the coastal and oceanic environment and the deep sea. After a brief introduction to each section outlining some characteristics of the zones, responses by marine organisms are dealt with under the main headings of resistance adaptations and capacity adaptations. The former include tolerance to changes in temperature and salinity, to desiccation and oxygen stress. Capacity adaptations are dealt with under headings such as perception of the environment, feeding and the related morphological and physiological mechanisms which ensure extraction of the necessary energy from the environment, how there is a metabolic response and what is des-

cribed as a physiological strategy reflected in oxygen utilization. Useful sections consider how circulatory systems react to stress and review osmoregulatory activities in respect to habitat preference. Reproduction and development are influenced in each zone by factors including food, salinity, temperature, oxygen, photoperiod and lunar cycles. The arrangements in the book of zones, responses and the various factors operating in the environment enable a reader to find his way to what he wants with ease. The chapter on the deep sea contains interesting material but was written before contributions at a recent conference (*Symp. Soc. Exp. Biol.*, **26**; 1972) on the effects of pressure on organisms could be included. The last chapter deals with pollution effects; thermal aspects, radionuclides, industrial wastes, pesticides are discussed and a striking electronmicrograph shows the damaging effects on the gill tissue of fiddler crabs after they have been maintained in 0.18 p.p.m. Hg for 6 weeks. A final short section considers the possible far reaching consequences of human manipulation of the marine environment. Successful aquiculture can only develop when our knowledge of the adaptations of potential food species will allow management and selection similar to those that helped agriculture. The text is usefully illustrated with numerous clear figures, tables and diagrams. It presents much information, occasionally in a somewhat staccato and condensed form but which cannot fail to be valuable to anyone studying physiological responses in marine creatures, even though as the authors themselves admit we do not yet understand why an organism lives where it does. R. J. HARRISON

Eating in Old Age

Nutrition in Old Age. Edited by Lars A. Carlson. Pp. 180. (Almqvist and Wiksell: Stockholm 1972.) Sw.kr. 50.

As stated in the introduction, few nutritionists are interested in the problems of old age and few gerontologists are interested in nutrition. This international symposium brings together some of the information available regarding the nutritional needs of the elderly and underlines the shortage of information, while at the same time emphasizing the difficulties in collecting evidence.

Dr W. T. C. Berry points out that epidemiologists generally require a minimum of 1,500 subjects while several of the papers indicate that comprehensive measurements of a few hundred elderly subjects call for a major effort. It is difficult to measure even food intake with any accuracy and much more difficult to establish the presence of mild degrees of undernutrition either

in individuals or groups. Body weight can be very misleading because of changes in the ratio of fat to lean body mass with advancing years. Certainly it is well known that energy output falls with age so that there is likely to be a fall in the intake of nutrients.

On the basis of work carried out both longitudinally on 650 males over the past 10 years, as well as by cross-sectional analysis, Dr N. W. Shock concludes that the fall in basal metabolism with age is simply a reflexion of the reduced amount of metabolizing tissue. His colleague Dr R. Andres shows that ageing results in reduced glucose tolerance, but there is no evidence on which to decide whether this is due to the appearance of diabetes or a non-pathological manifestation of ageing.

Drs Werner and Hambraeus of the University of Uppsala have investigated the digestive capacity of 700 old people and reported intolerance to fat and protein in amounts well tolerated by younger people, not associated with disease of the digestive tract. It is not clear whether this is due to decreased production of digestive enzymes or reduced absorption.

The average bone loss between middle life and old age is 15% of the skeleton. Senile osteoporosis, which affects both sexes from the age of 60, is associated with declining absorption of calcium and is partly reversible with vitamin D. Dr B. E. C. Nordin and his colleagues state that mild vitamin D deficiency causes malabsorption of calcium leading to osteoporosis, while more severe deficiency lowers the plasma calcium and leads to osteomalacia. An interesting suggestion was made during the discussion that evidence of the preventive properties of vitamin D might be derived from comparison of these bone disorders in the United States, where liquid milk is fortified with vitamin D. But in support of the contention that so little information is available in this whole field it was stated that fracture rates as a function of the population at risk are available only from the UK and Sweden.

The evidence for increased requirements of vitamins with old age is reviewed by Dr Sylvia Darke, who concludes that there is none. The difficulties are illustrated by the finding that while anorexia, insomnia and increased irritability are associated with early stages of thiamin deficiency and are common complaints of the elderly there is no evidence of a connexion.

One problem discussed by Drs Soremark and Nilsson is that of decreased taste acuity, salivary flow and loss of teeth which have a major effect on dietary selection, even if incomplete mastication has no effect on efficiency of digestion.

The final discussion where speakers

point out necessary fields of further research and unsolved problems is an extremely valuable part of the book. One of these problems is the association between longevity and restricted food intake; another is the longer life of women—the discrepancy in the US has risen from 2 years to 8 years since 1900 in spite of the greater prevalence of obesity in women (and the observation that obesity shortens life). Above all is the major problem of the relation between unusual or so-called abnormal biochemical parameters of nutritional status, health and longevity. What is "normal" has long been undefined: the greater divergences from average met in the elderly make the question even more difficult to answer.

ARNOLD E. BENDER

Gene Mapping

Gene Mapping in Laboratory Mammals. Part A. By R. Robinson. Pp. vii+151. (Plenum: London and New York, 1971.) $17.

THIS book, the first of a two-part work, represents a bold attempt to summarize the mathematical and statistical aspects of linkage estimation; but its usefulness must be questioned. For those with a modicum of mathematics, it could reasonably be argued that the existing literature is adequate. The bibliography of the present volume cites books on the mathematical aspects of linkage, and provides an entry to the primary literature, which is generally quite accessible. There is, however, a need to present the ideas to those without mathematical sophistication but who may have genes to map. Such people will not profit at all from this volume. Unless they understand maximum likelihood, for example, they become drop-outs on page 24, without learning even what it is all about. The introduction of matrices on page 29 is equally preemptory. In general, the mathematical presentation, though mostly elementary, is very inexplicit, and anyone with sufficient knowledge to follow the development of the topic in this book is at least well enough equipped to get along without it.

The book has its odd moments, as on page 36, where a simple statistical identity is credited to a well-known geneticist. And in a volume implying much tiresome computation, it is incongruous to find that Table 4.1 only lists some values of a simple function (badly misprinted in the title of the table) which is perfectly amenable to pencil-and-paper arithmetic. And so forth. In a more positive vein, the author draws attention to the difficulties of estimation when normal segregation is disturbed. This, as he points out, is a problem in practice though, I should have thought, one that is widely appreciated. What the uninitiated would have welcomed would be a clear exposition, in terms of worked numerical examples, of the methods of coping with messy data. Unfortunately, this volume has only one numerical example, and even that is hypothetical and trivial; it suffers further from a confusing misprint. Hopefully, more worked-out examples will be given in the forthcoming part B, which promises to examine "the accumulated data on linkage for most of the laboratory mammals and provides a comprehensive and up-to-date survey". The second part will therefore be eagerly awaited by many, and if its price is kept down because part A has been issued separately, then we need not question too closely a publication policy that yields two volumes where one might have done.

R. C. ROBERTS

Membranes and Impulses

Perspectives in Membrane Biophysics. Edited by D. P. Agin. (A Tribute to Kenneth S. Cole.) Pp. vii+317. (Gordon and Breach: New York, Paris and London, 1972.) £7.70.

THERE can be no room for doubt that the work of K. S. Cole has been of seminal importance in the field of nerve and muscle biophysics. It was he and Curtis who first showed in 1938 that the nerve impulse is accompanied by a large increase in membrane conductance. In 1949 he and Marmont gave the first descriptions of the voltage clamp technique that formed the basis of Hodgkin and Huxley's classical analysis of the impulse mechanism in 1952. Over a period of 40 years he has influenced a large number of the most important workers in the field. This volume contains sixteen papers written as a tribute to Cole on his seventieth birthday by former colleagues, students or admirers.

Some of the papers are based on work already published or take the form of a normal journal or review paper. In addition, however, there are some gems that have clearly been written specially for this volume because they concern particular problems that are uniquely, or almost uniquely, associated with Cole's name. To give two examples of these: R. D. Keynes discusses some reasons for investigating in more detail the relative constancy of the membrane capacitance established by Cole and Curtis in their impedance measurements; Adrian, Chandler and Hodgkin describe an elegant extension of what has come to be called "Cole's theorem" and its application to threshold measurements in skeletal muscle. These papers have very obviously been written in response to the invitation to contribute to this

Army Ants
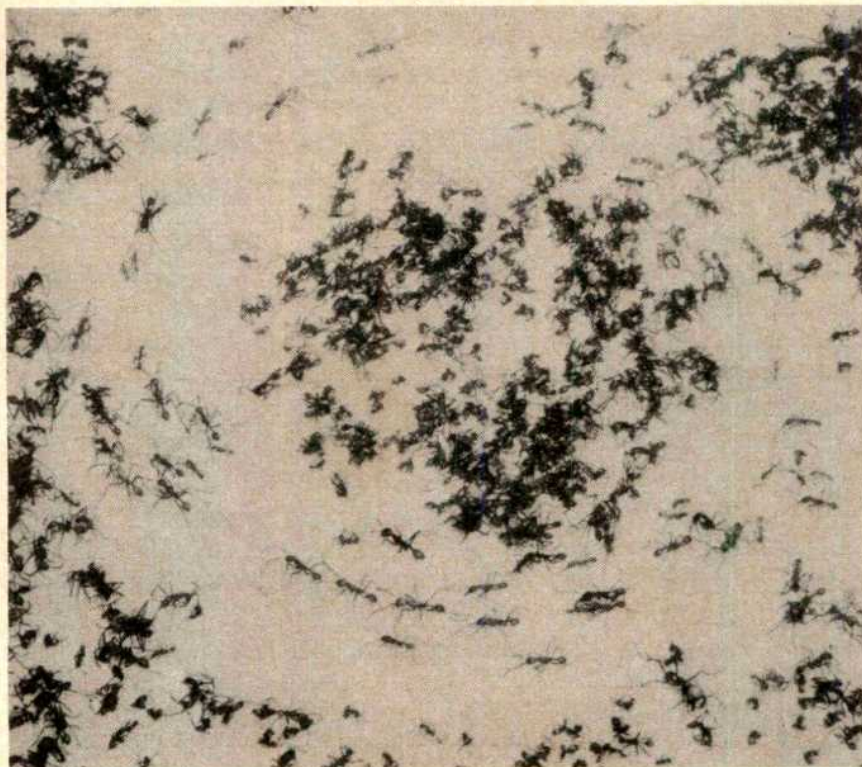
Circular column of the famous army ants studied by T. C. Schneirla, whose selected writings, on topics from social bonds to conceptual trends in comparative psychology, and including much about ants and other insect behaviour, are published by W. H. Freeman (*Selected Writings of T. C. Schneirla*, W. H. Freeman, San Francisco, 1972).

volume. All the papers, however, draw their connexions to Cole's work in perfectly natural ways, including in many cases descriptions of the way Cole had suggested or influenced the work. One obtains therefore an unusual view of the way in which one man has contributed directly or indirectly to the development of the field. The result is a fitting tribute to Cole, quite apart from being a valuable collection of papers on membrane biophysics.

D. NOBLE

Heredity for Laymen

Heredity in Humans. By Amram Scheinfeld. Pp. xvi+303. (Chatto and Windus: London, January 1973.) £2.50.

THIS is the fifth, or, according to one's classification, the ninth book by Scheinfeld aimed at explaining heredity to the layman, which began in 1939 with the publication of the very successful *You and Heredity.* It is not intended to compete with the more voluminous and detailed *Your Heredity and Environment* of 1965, but may be regarded as an up-to-date successor to *The Human Heredity Handbook* published in 1956.

The approach is "pragmatic" rather than analytical or technical, attempting to answer many questions asked by laymen in laymen's language: for instance why children resemble their parents, but not always; in what way men and women "naturally" differ; how certain diseases and defects are inherited; how ethnic groups differ in their genes; what part heredity plays in intelligence, talent, behaviour, personality and sex life.

Most offered explanations are roughly correct, but the method of presentation is often unnecessarily crude and also too dogmatic. It is probably not very useful to describe dominant genes as "bully genes", genes producing various oddities as "freak genes", genes working unexpectedly and only under some circumstances as "temperamental genes"—genes of late onset as "Rip van Winkle genes". Some curious concepts also should be pointed out. Why, for instance, call some Indians, Arabs and North Africans "dark skinned whites"?

The situations used for the illustration of the author's points of view in respect of race, intelligence differences and similar problems are mostly chosen from the orbit of metropolitan New York and sometimes a certain bias seems to have prevailed; it is, for instance, curious not to mention the Germans among the people who contributed to music. Nevertheless, if laymen do not take the text as gospel—which, unfortunately, some of them tend to do—this book can do a good deal in counteracting antiquated and bigoted assertions. H. KALMUS

Common Toad
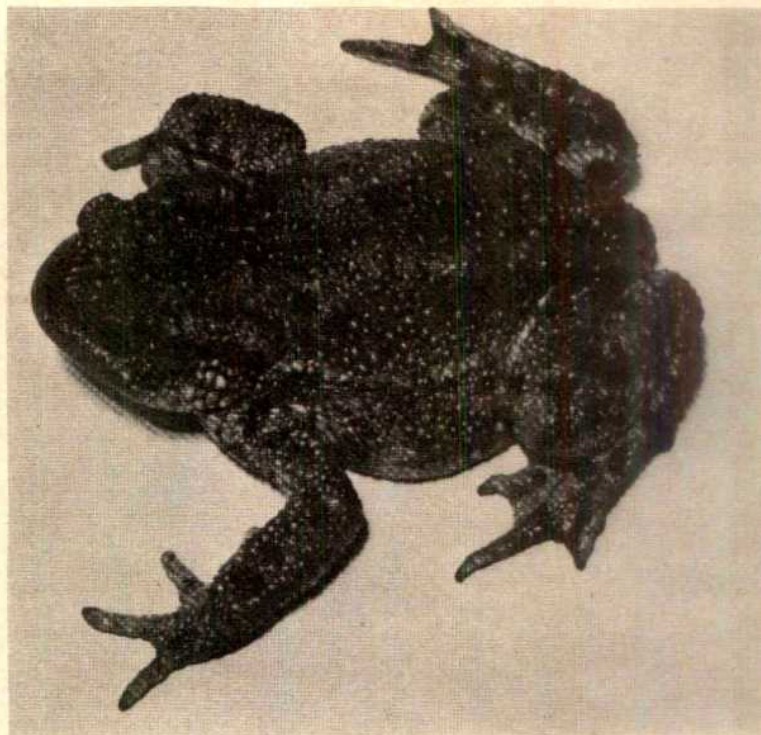
A particularly large female toad illustrating the adaption of amphibians to relatively dry environments in *Amphibians,* by J. F. D. Frazer (Wykeham Publications, London, 1973).

Diseases of Plants

The Principles of Plant Pathology. By S. A. J. Tarr. Pp. 632. (Macmillan: London and Basingstoke, September 1972.) £10.00.

PLANT pathology, whether interpreted narrowly or as broadly as in this book, is to plants what the whole of medicine and veterinary science is to man and animals. It is therefore not surprising that Butler and Jones's monumental textbook *Plant Pathology* of 1949 is said to have marked the end of an era. Increasingly the subject requires several multi-author-volumes. The facts about individual pathogens, diseases and ways to control them seem best presented in loose pamphlets sold on a subscription basis, as some are through the Commonwealth Mycological Institute. In this way every topic can have specialist treatment and be revised separately whenever necessary. Review journals satisfy a further part of the need, but neither pamphlet nor review would provide the "thorough background to all aspects of plant pathology" which this book is claimed to do. The task was certainly ambitious because, with only a brief history of plant pathology written by Dr Ainsworth and several helpers who checked other chapters, Dr Tarr undertook work that recently

occupied three volumes of contributions by many authors. Struggling no doubt against severe limitations of space and price the author has produced an up-to-date book of pleasing format, with few errors but with illustrations that are rather scanty and often disappointingly presented.

Many apologies for brief accounts show that Dr Tarr knew how much he was omitting. Estimates of the soundness of his choice will probably differ depending on the interests and experience of his readers. So will opinions of the wisdom of mentioning rodents, birds and molluscs as if they, as well as some angiosperms and chemical excesses or deficiencies, should be regarded as plant pathogens. However, here as elsewhere, Dr Tarr plainly states the alternatives possible and the consequences that each may incur. He rarely obscures our ignorance under a heap of terminology, but occasionally invents terms for which the need is doubtful. Dr Tarr states that he has aimed his book at students, and novices will appreciate the wide scope of the book and be glad of the reminders that come in the rather repetitious and overlapping early chapters, some so abbreviated that they contain little but lists and generalizations. Surely a treatment of the major nutrients (NPK) that only

occupies two and a half pages and three references cannot do them justice. Nevertheless teachers will applaud the book for many references, some so recent that they were probably added in proof, and for the author's habit of quoting major references at the end of sections and of the book. Students lucky enough to borrow the book, for sadly few can afford personal copies, will find it an excellent "thought-saving" source for essays.

However, students grow into practitioners of plant pathology and they will often find the six hundred pages contain disappointingly brief answers to their inquiries or conclude their special interests have too little attention. Is it right that any comprehensive book on the principles of plant pathology should dismiss viruses and mycoplasmata with thirty-six pages and an apology? Although "root diseases" are mentioned often, the chapter devoted to them is only a third of that on viruses and about half that on "non-parasitic agents". The chapters dealing with infection, attack and defence mechanisms are more satisfying and the author is to be complimented on recognizing both that there is an epidemiology of root diseases and the importance of pathogen and host carry-over in starting epidemics. The latter theme is emphasized again through disease control by sanitation and cultural practices. Other chapters contain good summaries of existing knowledge on dispersal, forecasting and assessing diseases or controlling them by fungicides, resistance, quarantine and so on. However, I am still waiting for the book that not only describes the principles of plant pathology as an academic subject, but also stresses how disease control must be fitted into changing agricultural systems and show benefits greater than its cost.   J. M. HIRST

recent years and this series of books is intended for specialists as well as for students.

The relevant chapters account for 80% of the whole text (85% if the introductory and concluding chapters are excluded) and their share of the references is 78% (80%). They constitute admirable reviews but the remainder seem too sketchy even for junior students. Chapter 3 on the biochemistry of the pigments seems particularly light, and also adrift, no doubt because the "visual-effect" functions of the integumental chromes depend essentially on biophysical properties and mechanisms, chemical properties being largely irrelevant.

It should be re-emphasized that the structure and development of chromatophores and their organelles are well reviewed, with excellent illustrations and that the hormonal and nervous controls of vertebrate chromatophores are very critically discussed: some may feel that the authors are hypercritical concerning the significance of melatonin. There is a generous bibliography, mainly of recent references, in line with the aims of the series, but what a pity such a long list is not arranged alphabetically, particularly as there is no author index.

In spite of the weight of the authors' summing up, a number of leading questions must be considered still sub-judice. Many will wear Sir Lancelot's favours in the tournament of hormonal control and the albedo school will question whether a pineal–incident light response can be independent of the pituitary–background response.
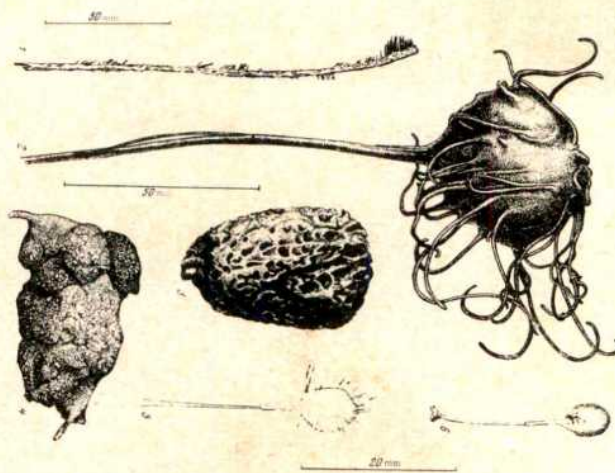
A. E. NEEDHAM

Nobel Biology

Nobel Lectures, Physiology or Medicine. 1963–1970, including Presentation Speeches and Laureates' Biographies. Pp. x+273. (Elsevier: Amsterdam, London and New York, 1973.) Dfl. 110; US$ 34.50.

THESE Nobel Lectures are an enjoyable if expensive way of keeping up with the major advances of biology and medical science. Needless to say, the authors are an all-star cast—(in order of appearance) Eccles, Hodgkin, Huxley; Bloch and Lynen; Jacob, Lwoff and Monod; Rous and Huggins; Granit, Hartline and Wald; Holley, Khorana and Nirenberg; Delbrück, Hershey and Luria; Axelrod, von Euler and Katz.

The lectures are about equally divided between molecular biology in its now accepted sense, expounded by many of its founders, and neurosensory physiology, a subject that was deeply molecular long before many of the disciplines now eager to be so described. The lectures are remarkably good reading because the authors have obviously taken considerable pains with them. The citation or presentation speeches have also been very carefully prepared and add greatly to the value of the volume. These Nobel Lectures could be really useful reading for students of medicine or life sciences from whom future laureates must be recruited. It is a pity that some great Foundation at its wits' end to know how to spend its money does not subsidize their publication in paperback, so putting the lectures within the means of those who would benefit most by reading them.

P. B. MEDAWAR

Chromatophores

Chromatophores and Color Change: The Comparative Physiology of Animal Pigmentation. By Joseph T. Bagnara and Mac E. Hadley. Pp. xvi+202. (Prentice-Hall: Englewood Cliffs, New Jersey, January 1973.) £6.

NOTWITHSTANDING the jacket's claim, "a balanced review of all facets", there is a strong bias towards the authors' own fields of research, as they are first to emphasize. Some readers will question whether so strong a bias is justified under the very broad title. Certainly the authors' research fields—the micro-anatomy and development of chromatophores, and their behaviour as effector organs in vertebrates — have been among the most progressive in

Marine Fauna

Inhabitants of the Kurile-Kamchatka Trench, as revealed in the thirty-ninth cruise of the Vityaz : one of the drawings from *Fauna of the Kurile-Kamchatka Trench and its Environment,* edited by V. G. Bogorov and distributed for the Academy of Sciences of the USSR and the Israel Program for Scientific Translations by Wiley (Chichester, 1973).

in the original diploid micronucleus. The macronucleus divides into two bodies to complete the process of macronuclear formation, and the cell resumes vegetative reproduction with a maximum cell cycle time of about 8 h.

The loss of DNA that occurs during the vesicle stage of the macronuclear anlage is apparently restricted to particular nucleotide sequences[5]. The buoyant density profiles of micronuclear and macronuclear DNAs are compared in Fig. 4. The density profile of micronuclear DNA has several peaks; a computer analysis has indicated that the profile is probably made up of a minimum of four density components with peaks at 1.699, 1.701, 1.704 and 1.709 g cm^{-3}. In contrast, the profile for macronuclear DNA has a single component with a peak density at 1.701 g cm^{-3}. Presumably the nucleotide sequences present in the macronuclear DNA are represented in the micronuclear DNA only by the component with a peak density of 1.701 g cm^{-3}. Assuming the presence of four density components in the micronuclear DNA, the computer analysis indicates that the DNA with a density of 1.701 g cm^{-3} accounts for less than 10% of the total micronuclear DNA. The melting profiles of macronuclear and micronuclear DNAs show essentially the same phenomenon (Fig. 5). Macronuclear DNA melts as if it were a single component, whereas micronuclear DNA melts as if it contained several components of different base composition.

We conclude that the absence in the macronucleus of several density (or melting) components of DNA, which account for more than 90% of the total micronuclear DNA, must be a consequence of the observed destruction of 93% of the DNA in the polytene-like chromosomes. This does not necessarily mean that only 7% or so of the different sequences present in micronuclear DNA are retained in the macronucleus; some of the destroyed DNA might represent multiple copies of one or a few nucleotide sequences. The fact that much of the micronuclear DNA absent in the macronucleus forms discrete density components in CsCl density gradients suggests the pres-
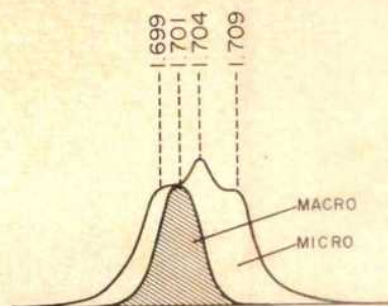

Fig. 4 Buoyant density profiles in CsCl for micronuclear DNA (above) and macronuclear DNA (below). Micronuclear DNA consists of at least four density components with peaks at about 1.699, 1.701, 1.704, and 1.709 g cm^{-3}. Macronuclear DNA consists of a single component with a density peak at 1.701 g cm^{-3}.

ence of repetitious DNAs, since these components might be analogous to the satellite DNAs demonstrated in many higher eukaryotes. In any case, the buoyant density and melting profile data indicate a major reduction, if not elimination, of some fraction of the micronuclear nucleotide sequences during formation of the macronucleus.

The most direct, quantitative way to measure the reduction in nucleotide sequences in the macronucleus would be to compare the renaturation rates after heat denaturation of the DNAs from the two kinds of nuclei. For several technical reasons micronuclear DNA is difficult to prepare from *Stylonychia* in adequate amounts for this kind of analysis, but it probably can be done. Macronuclear DNA is easily obtained, and this DNA renatures with a Cot 1/2 about twenty times greater than does the DNA of *E. coli* (unpublished results of D. M. P. and C. J. B.). The renaturation pattern for macronuclear DNA contains no indication of sequence repetition.

Nothing is known about the mechanism by which the destruction of DNA in the macronuclear anlage is achieved.
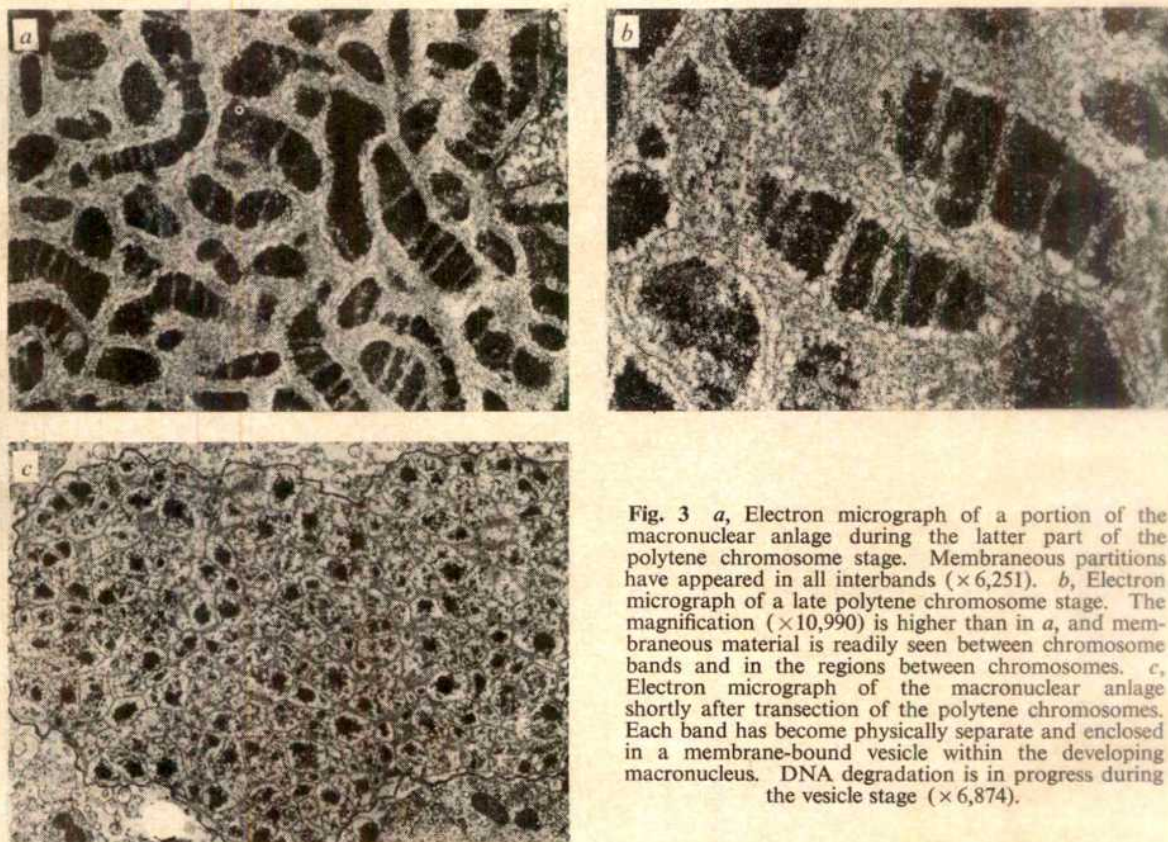

Fig. 3 *a*, Electron micrograph of a portion of the macronuclear anlage during the latter part of the polytene chromosome stage. Membraneous partitions have appeared in all interbands ($\times 6,251$). *b*, Electron micrograph of a late polytene chromosome stage. The magnification ($\times 10,990$) is higher than in *a*, and membraneous material is readily seen between chromosome bands and in the regions between chromosomes. *c*, Electron micrograph of the macronuclear anlage shortly after transection of the polytene chromosomes. Each band has become physically separate and enclosed in a membrane-bound vesicle within the developing macronucleus. DNA degradation is in progress during the vesicle stage ($\times 6,874$).
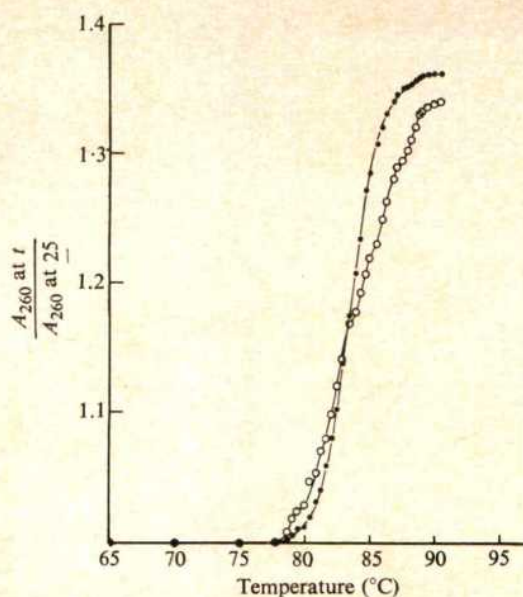
Fig. 5 Melting curves for micronuclear DNA (○) and macronuclear DNA (●). Macronuclear DNA melts with a sharp transition in hyperchromicity, indicating the presence of a single component. Micronuclear DNA melts with a complex pattern, indicating the presence of several components.

The elimination of DNA must be controlled in some way to assure the retention of essential nucleotide sequences because it is the macronucleus that runs the vegetative life of this cell. Nuclease action must therefore be specifically directed toward certain nucleotide sequences, but the basis of this specificity is completely unknown. This specificity apparently does not involve 5′ methyl cytosine residues in DNA because neither micro- nor macronuclear DNAs of *Stylonychia* contain a detectable number of such residues (personal communication from D. Brown).

From the cytological standpoint the two simplest hypotheses to explain the elimination of DNA are as follows. (1) All the DNA in 93% of the vesicles is destroyed, and all the DNA in 7% of the vesicles is retained. (2) Each of the vesicles formed from the polytene-like chromosomes loses 93% of its DNA. It is not possible at present to rule out either of these hypotheses.

If the decrease in DNA in *Stylonychia* takes place by the degradation of 93% of the DNA in each band (vesicle), then the remaining 7% of the DNA might reasonably be expected to be of low molecular weight. The pieces of DNA produced by the transecting of the polytene chromosomes would be further reduced in size by the 93% degradation of DNA. Evidence that the macronuclear DNA is small has already
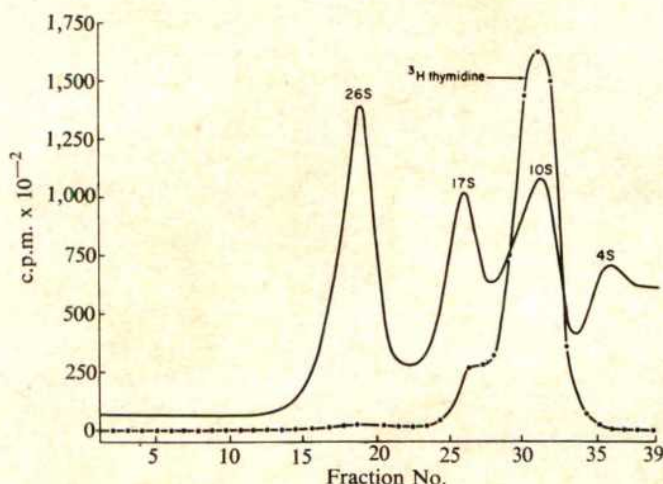

Fig. 6 Sucrose gradient sedimentation of nucleic acids from isolated macronuclei. The absorbance profile shows ribosomal RNA (26 and 17S), 4S RNA, and DNA (10S). The cells were labelled with ³H-thymidine for several cell cycles, and all radioactivity is contained in the 10S peak plus a small 14S shoulder.
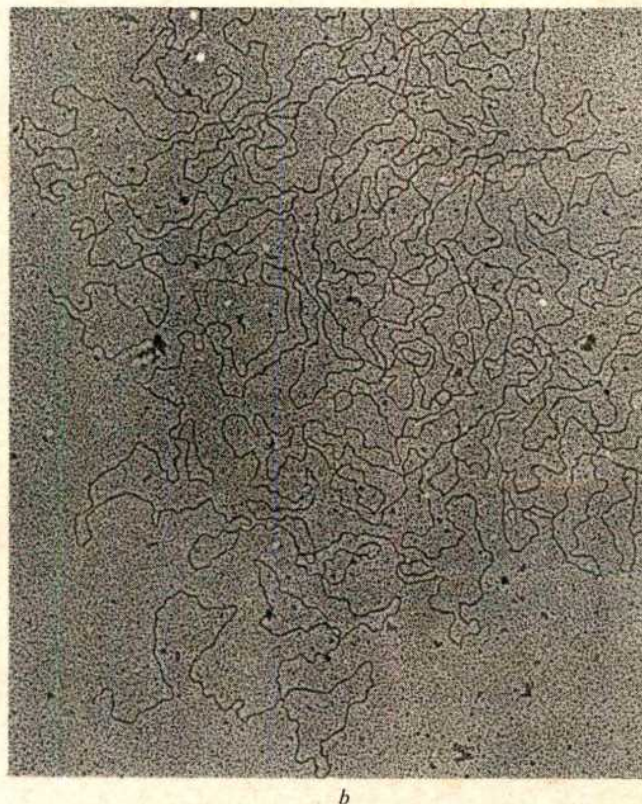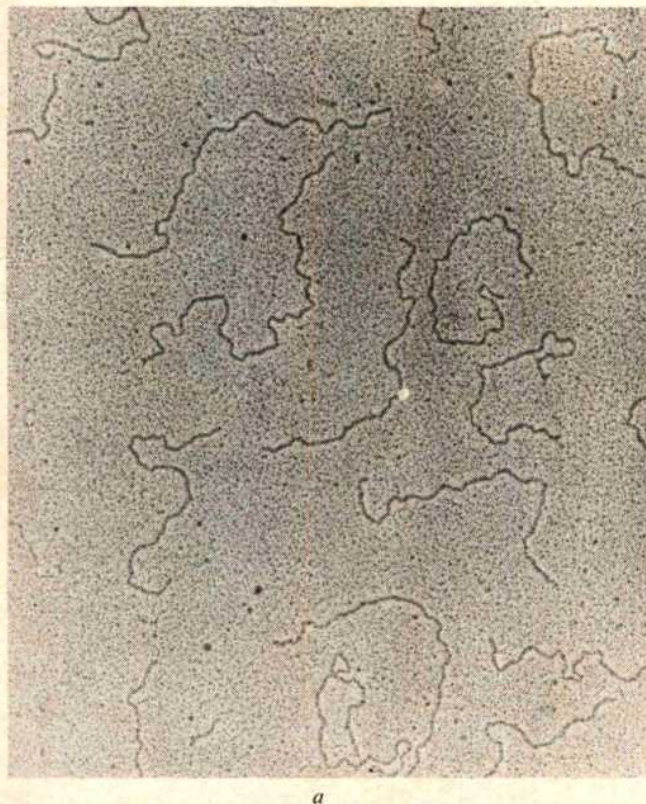

Fig. 7 *a*, Electron micrograph of macronuclear DNA. All the DNA is in short pieces, with an average length of 0.8 μm (× 49,000). *b*, Electron micrograph of micronuclear DNA. All the DNA is in long pieces, and free ends are scarce (× 20,000).

been published[6]. First, macronuclear DNA sediments with a peak of about 10S in a neutral sucrose gradient (Fig. 6). The 10S peak has a shoulder on the heavier side, and occasionally this shoulder is resolved as a peak of 14S. Micronuclear DNA sediments with S values between 20 and 100 depending on the amount of shearing that occurs during preparation. Various tests (described in Prescott *et al.*[6]) indicate that the low S value for macronuclear DNA is not due to degradation during DNA isolation.

In the electron microscope, DNA from the macronucleus appears as small pieces from 0.2 to 2.2 µm long (Fig. 7a). In contrast, micronuclear DNA from the same cell lysate occurs in much longer pieces—usually too long to measure, since free ends of molecules are not common (Fig. 7b). The histogram in Fig. 8 shows the distribution of size of macronuclear DNA molecules. The distribution is bimodal with a major peak of DNA pieces with a mean size of about 0.75 µm and a minor peak of DNA pieces about 2.0 µm, the major and minor peaks presumably reflecting the two peaks (10S and 14S) observable in sucrose gradients.

The following information is available about the pieces of macronuclear DNA. When macronuclear DNA is heated, in the presence of formaldehyde, to the temperature at which hyperchromicity just begins to appear, every piece of DNA melts at one end[7] (Fig. 9); no pieces have ever shown melting at both ends. The melting is interpreted to reflect a higher content of adenine and thymine in one end of each molecule than is present throughout the main part of each molecule. At the very least, this observation shows that each piece of macronuclear DNA has a polarity, and suggests that all pieces share a common property at one end.

The pieces of macronuclear DNA also bind RNA polymerase[7]. One molecule of RNA polymerase (from *Bacillus subtilis*) is bound at the end of each DNA piece when the binding reaction is performed in the absence of pyrimidine nucleotide triphosphates (Fig. 10). Binding has never been observed at both ends or at internal regions of molecules. This means that one end of each piece of macronuclear DNA has a high affinity for RNA polymerase. Whether the RNA polymerase binds at the end that is richer in adenosine and thymidine remains to be proven. Clearly the experiments
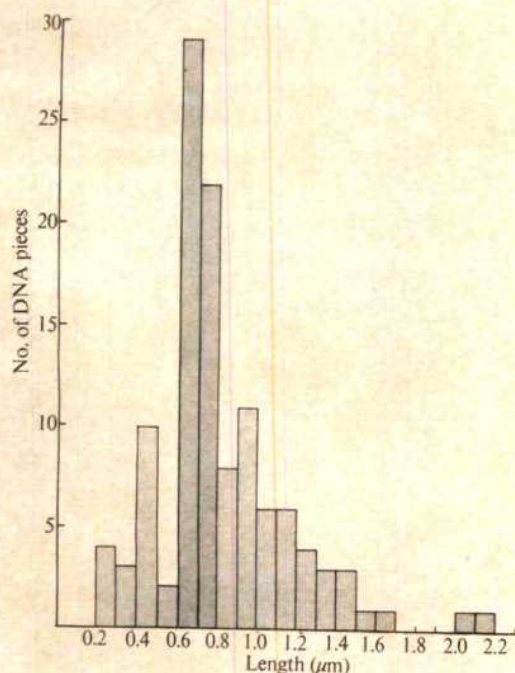

Fig. 9 Electron micrograph of macronuclear DNA brought to the beginning of melting in the presence of formaldehyde. Each piece of DNA has a melted region at one end.
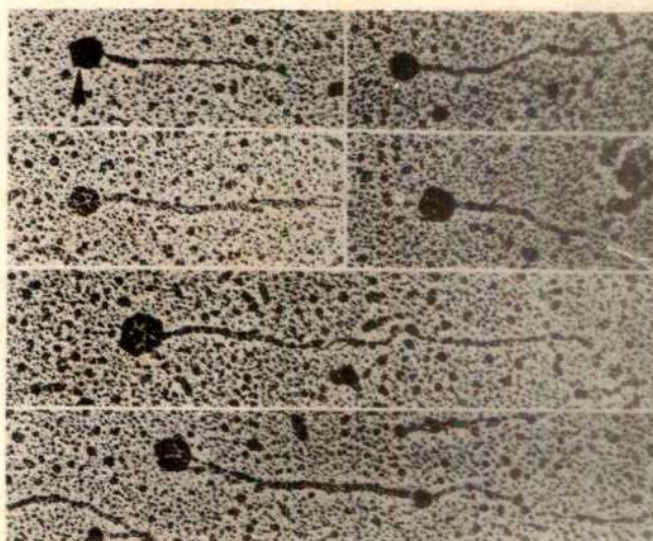
Fig. 10 Electron micrograph of macronuclear DNA complexed with RNA polymerase of *Bacillus subtilis*. Each piece of DNA binds an RNA polymerase molecule at one end.

confirm that all the macronuclear DNA molecules possess a polarity and that all the molecules probably have a property in common at one end. We do not know, of course, whether the binding of RNA polymerase of *B. subtilis* provides an identification of the natural binding site of the *Stylonychia*'s RNA polymerase to macronuclear DNA; RNA polymerase from *B. subtilis* and *E. coli* transcribe macronuclear DNA quite efficiently (unpublished results of D. M. P. and M. R. Lauth).

Finally, the bimodality on the sizes of macronuclear DNA is significant for the following reason. *Stylonychia* synthesizes an RNA precursor molecule with an S value of about 34 in a sucrose gradient. The 34S precursor molecule is processed into a 26S and a 17S molecule of ribosomal RNA. The 34S molecule must have a molecular weight of 2 to 2.5 million. The DNA duplex acting as template for synthesis of the 34S precursor molecule must therefore have a molecular weight of 4 to 5 million. The minor peak of macronuclear DNA at 14S, presumably corresponding to the 2 µm pieces (molecular weight of 4 million) of DNA seen in the electron microscope, has DNA in the right size range to code for ribosomal precursor RNA. Ribosomal RNA of *Stylonychia* has been hybridized with DNA of *E. coli*, with the 10S DNA, and the 14S DNA of the macronucleus. The results (Fig. 11) show a slight amount of binding of the ribosomal RNA to DNA of *E. coli*

Fig. 8 The distribution of length of macronuclear DNA measured in the electron microscope. The larger pieces are believed to reflect the small 14S shoulder seen in sucrose gradients.
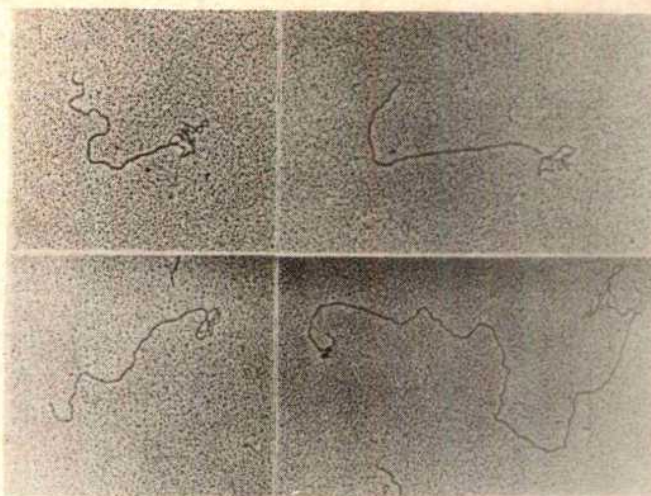
and to 10S DNA, but pronounced binding to 14S DNA. The small amount of binding to 10S DNA may represent contamination of 10S DNA with 14S DNA, since the two size classes are difficult to separate cleanly on a sucrose gradient. About 7% of the 14S DNA hybridizes with ribosomal RNA.

The three observations, melting of ends of molecules, binding of RNA polymerase, and presence of the ribosomal genes in the minor 14S peak, support the hypothesis that the small pieces of macronuclear DNA are the functional, transcriptional units of the macronucleus of the living cell.

The average piece of DNA (0.75 μm) could theoretically code for 750 amino-acids. Since this would imply an unusually large polypeptide, we must assume that less than half of each piece of DNA codes for amino-acids (300 amino-acids would be a more usual size of a polypeptide), or alternatively, many pieces of DNA must code for two or three different polypeptides.

The pieces of macronuclear DNA contain all the genetic information needed to support cell growth and reproduction, as well as all of the metabolic functions of the vegetative cell. This is known because more than 99% of RNA synthesis occurs in the macronucleus during vegetative growth, and the trace of RNA synthesis that occurs in the micronucleus is known to be expendable; amicronucleate strains of *Stylonychia* are easily obtained, and these proliferate for many cell generations without the benefit of micronuclear DNA. Amicronucleated clones do senesce and die sooner, however, than do micronucleated clones.

The observations on *Stylonychia* described here suggest a model of chromosome organization in which a few per cent of the DNA in a band constitutes the genetic locus, and the remaining 93% or so is of unknown significance. The situation is summarized in Fig. 12. The "non-gene" DNA is designated here as "spacer" for lack of information about its possible significance. Each gene locus (or group of gene loci) is separated from the neighbouring gene loci by spacer DNA. During the vesicle stage of the macronuclear anlage transection of the chromosome will occur such that each vesicle contains a gene locus and a stretch of spacer DNA. The arrangement shown in Fig. 12 is similar to the spacer-gene situation present in the DNA containing ribosomal genes. We also note that it has similarities to the structure of the chromosome proposed
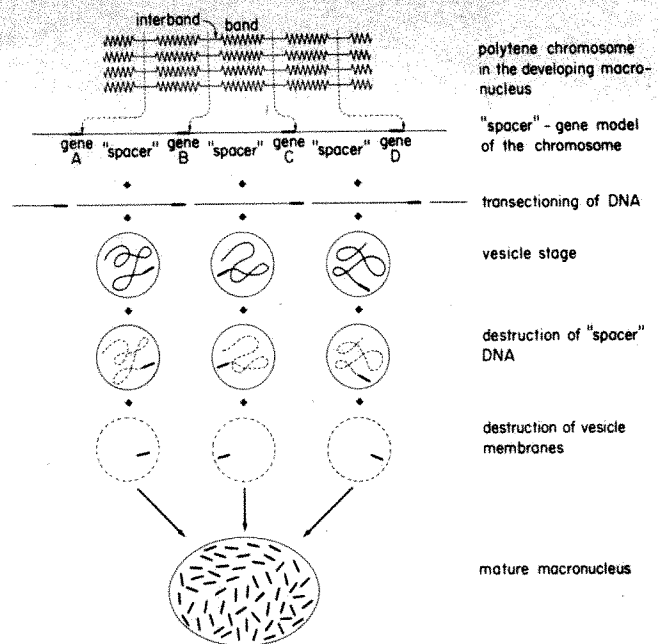

Fig. 12 A scheme to explain the derivation of the gene-sized pieces of DNA in the mature macronucleus from the chromosomes of the micronucleus. The micronucleus goes through several rounds of DNA replication to produce the polytene chromosomes of the early macronuclear anlage. Each band of the polytene chromosomes in the macronuclear anlage is assumed to represent a single genetic locus. The polytene chromosomes are transected between successive bands as shown in Fig. 3. The polytenic copies of DNA in each band become enclosed in a vesicle (Fig. 3). Only one copy is shown in each of the three vesicles in the drawing. Most of the DNA in each vesicle (band) is considered to consist of a spacer that separated the gene copy in one band of a chromosome from the gene copy in the next band. Destruction of the "spacers" occurs in the vesicle stage and is assumed to account for the degradation of 93% of the DNA in the anlage. Only the structural genes with control regions, accounting for 7% of the original chromosomal DNA, are preserved. Destruction of the vesicle membranes produces a macronuclear anlage containing gene-sized pieces of DNA. This DNA is replicated many times to produce the DNA-rich, mature macronucleus.
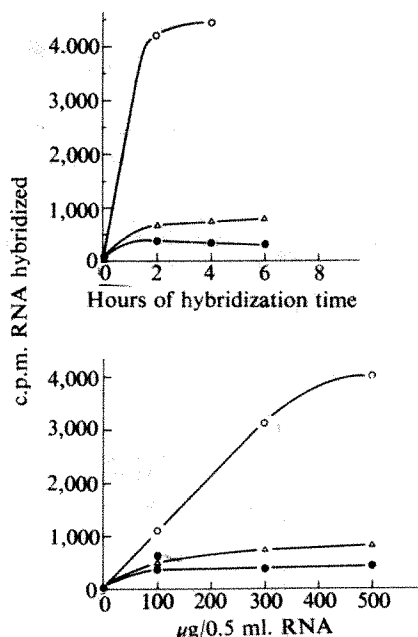
by Crick[8]. In the model in Fig. 12 the structural genes are suggested to occupy the interbands, but we have no direct evidence on this point.

The results so far indicate that the macronucleus of *Stylonychia* is a sac of DNA pieces that correspond to little more than single genes for ordinary-sized proteins. Each gene is represented by hundreds of copies. This situation may prove useful in the study of gene structure and function, particularly if various transcription units can be prepared in pure form.

The further study of the steps by which macronuclear DNA is derived from micronuclear DNA may tell us whether the chromosome model in Fig. 12 is correct. We are currently mapping the location of macronuclear DNA sequences within micronuclear DNA as a test of our concept of the chromosome and its processing in *Stylonychia*.

Fig. 11 Hybridization of ribosomal RNA of *Stylonychia* with the 10S (△) and 14S (○) fractions of macronuclear DNA and with DNA of *Escherichia coli* (●). The ribosomal RNA complexes slightly with DNA of *E. coli* and slightly more with the 10S DNA of *Stylonychia*. Ribosomal RNA complexes to a much greater extent with the 14S DNA fraction.

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LETTERS TO NATURE

PHYSICAL SCIENCES

Post-Occultation Reception of Lunar Ship America Radio Transmission

THE reception of radio signals from the orbiting lunar spaceship America after its occultation behind the lunar limb is a confirmation of results reported for the Apollo 15 ship Endeavour[1]. Similar observations arranged with the lunar command module during the Apollo 16 mission were unsuccessful because transmissions from the command module did not occur while the Moon was above our horizon.

The transmitter used for communication between the lunar command module and the lunar landing party was turned on almost continuously during a period of lunar orbiting between 1755 GMT, December 14, and 0400 GMT, December 15, 1972. The frequency of this transmission was 259.7 MHz with an audio signal at times impressed on the carrier. This transmission was intercepted by a special receiver attached to the 150-foot radio telescope of the US Air Force Cambridge Research Laboratory. This instrument is located at Sagamore Hill near Hamilton, Massachusetts, USA (latitude 42° 37′ 55.6″ N; longitude 70° 49′ 04.5″ W).

The spacecraft transmitted during most of the time the Moon was above the local horizon. Post-occultation signals were received when the Moon was near the local zenith. This high lunar altitude facilitated the reception and the signal strengths were much greater than on previous flights.

Occultation of the signal occurred at 0143:36 GMT, December 15, 1972. The signal did not immediately go to a zero level; it seemed to go to zero at approximately 0144:02 GMT and reappeared at 0144:12 GMT, persisted for 52 s, and finally disappeared at 0145:04 GMT. This behaviour indicates a dependence of the post-occultation signal on the exact topography of the lunar surface beneath the spacecraft.

Because the altitude of the Moon was higher than on previous flights, our signal strength was correspondingly greater, and we observed the Fresnel patterns that characteristically accompany occultation. When the signal reappeared, its level was approximately 20 db above noise (as shown by digital voltage recordings). The pen-recorded chart appears in Fig. 1. The AM and FM magnetic tapes and digital sampling of receiver output voltage provide alternative records, and an oscilloscope gave visual and photographic reception.
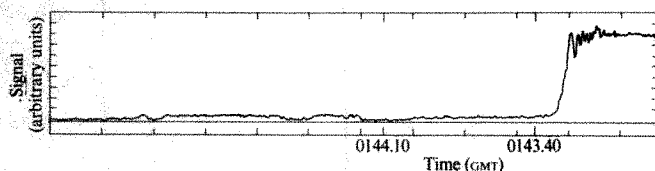

Fig. 1 Record of receiver response (1 division≡10 s).

The height of the America's orbit above the lunar surface was about 96 km at the time of occultation and was reasonably uniform thereafter. The occultation of the Moon ship occurred during 154° of its orbit relative to the lunar centre. During the elapsed time between the occultation and the disappearance of the signal, the ship traversed about 134 km of the lunar surface. The actual path of the signal was about 6 km less than this figure because the orbit of the ship was inclined to the line of sight to the Earth.

The surface distance traversed between the time of occultation and the time of disappearance of the signal projected on the signal path to the Earth is about 97 km. The effects of libration were insignificant.

Other results from this experiment, such as the possible significance of signals received during the other two occultations, are awaiting further reduction of the data.

Several possibilities for explaining such results have been considered[1-3], including refracted waves through the limb of the Moon or lunar surface waves. The immediate continuation of the signal after occultation favours the surface-wave explanation.

We thank the US Air Force Cambridge Research Laboratory for the use of the telescope, Dr Jules Aarons and the operators for assistance, and Dr Edward Lilley and Mr Hays Penfield of Harvard College Observatory for the use of their equipment and for many discussions. We also express our appreciation to NASA and the crew of Apollo 17 for their cooperation.

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Cariaco Trench: Oxidation of Organic Matter and Residence Time of Anoxic Water

THE Cariaco Trench is located on the Caribbean shelf of Venezuela and has a maximum depth of 1,400 m. The surrounding shelf is nowhere deeper than 150 m, thus separating the deep water of the trench from that of the Caribbean. The deep water of the trench is devoid of dissolved oxygen[1]. Between the sill depth and 500 m both temperature and salinity decrease, resulting in a slight increase in density which stabilizes the water column somewhat precariously. Below 500 m the water is uniform and well mixed. Such anoxic basins are critically dependent on the balance between supply of organic matter and renewal of the deep water. Although the sediments indicate that at least the deep part of the basin has been permanently anoxic for thousands of years[2] the relatively small density gradient may facilitate renewal of the deep water on a much shorter time scale. Estimates of the residence time vary between 100 and 2,000 yr (refs. 1,3). Data resulting from a cruise of RV Atlantis II in July 1971 provide a way of assessing the
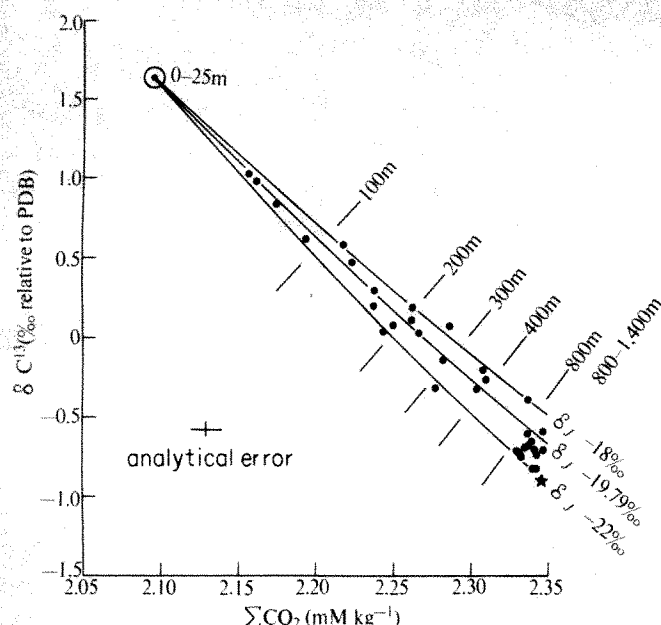
Fig. 1 Amount and $\delta^{13}C$ of total dissolved inorganic carbon in waters of Cariaco Trench. Curves signify addition of carbon having given $\delta^{13}C$ (δ_j) to mean surface water. *, Mean deep water in absence of methane formation. Total dissolved inorganic carbon was extracted from the water samples by acidification and gas sparging in a vacuum system[14]. After purification and drying, the liberated CO_2 was measured volumetrically and then transferred to a mass spectrometer for isotope analysis. The maximum extent of the analytical error in both kinds of determination is indicated by the error bars in the lower left corner of the figure. The points shown represent samples collected at several stations in the trench. They were superposed in one figure because no significant systematic differences between stations were detected and no single station covered the entire water column in sufficient detail. The uppermost point, labelled 0–25 m, is the mean of individual measurements of six samples from the surface waters; the values were combined in order to eliminate spatial and temporal variations commonly encountered in surface waters. ΣCO_2 is total dissolved inorganic carbon, $\delta^{13}C$ (‰) = [(($^{13}C/^{12}C$) sample/($^{13}C/^{12}C$) standard) − 1] × 1,000, the standard being Pee Dee belemnite (PDB) carbonate.

origin and oxidation of organic matter in the trench and the renewal rate of the deep water.

Measurements of $\delta^{13}C$ and ΣCO_2 on water samples covering the entire depth range of the Cariaco Trench are shown in Fig. 1. Both $\delta^{13}C$ and ΣCO_2 show an orderly progression of values from the surface to the deep water of the trench, through the interface between oxygenated and anoxic waters, which was commonly encountered between 250 and 300 m. This progression is the result of the accumulation of oxidized organic carbon in the water column of an anoxic basin[4]. From 800 to 1,400 m no further change can be detected, however, nor for temperature, salinity and other chemical constituents[1,5]. In Fig. 1, I also show the trajectories for the addition of CO_2 of three different isotopic compositions (δ_j) to the mean surface water. The trajectory $\delta_j = -19.7‰$ represents the addition of carbon having the $^{13}C/^{12}C$ ratio of the bulk cell carbon of plankton inhabiting the surface water (0–100 m) in the area of

the Cariaco Trench. In spite of the scatter of the data points it seems that, at least to a depth of 400 m, the data fit quite well the addition of oxidized plankton carbon and certainly fall between the two extremes shown. Part of the scatter may be real. There are minor, seemingly random, station-to-station differences; the scatter in the 200 to 300 m interval may be related to the undulating nature of the O_2-H_2S interface or possibly to chemosynthetic carbon fixation near the interface. Much of the irregularity, however, may be caused by analytical error. Data from below 800 m, however, not only cluster very closely but also, with one exception, indicate the addition of carbon of a ^{13}C content lower than of plankton carbon. The difference between mean surface water and mean deep water corresponds to the addition of 0.244 mmol CO_2 (kg water^{-1}) having a $\delta^{13}C$ of $-21.0‰$ ml.$^{-1}$. Such carbon is depleted in ^{13}C relative to plankton carbon but is still somewhat enriched relative to the bulk organic carbon contained in surface sediment of the deeper parts of the trench. For this material $\delta^{13}C$ is $\sim -22^{-1}‰$.

Several processes may cause deviations in the deep water from the trajectory described by addition of oxidized plankton carbon to the ΣCO_2. Because measurements of ΣCO_2 and $\delta^{13}C$ can reveal only the sum of all possible effects, I cannot rule out a priori any processes which may result in changes different from those observed because they may have been masked or cancelled by others. The principal processes to be considered are carbonate solution or precipitation, methane formation, fractionation during oxidation, and introduction of organic matter derived from the continent. Chemosynthetic fixation is not likely to be significant at this depth.

Part of the observed deviation could be produced by carbonate precipitation in the deep anoxic waters which would result in the removal of CO_2 enriched in ^{13}C from the water; but the sediments show no evidence for this. Nor is there any indication of carbonate solution which would result in the addition of heavier carbon to the ΣCO_2. (Bulk carbonate in the surface sediment has a $\delta^{13}C$ of $+1.2‰$). V. J. Linnenbom and J. W. Swinnerton (unpublished) measured methane concentrations between 0.1 and 0.15 ml. l.$^{-1}$ below 800 m in the Cariaco Trench. Because bacterial methane formation utilizes principally CO_2 (ref. 6) and the methane formed is strongly depleted in ^{13}C relative to the source material[7], this process will influence both ΣCO_2 and $\delta^{13}C$ in deep water. If the methane formed is isotopically similar to that formed in the Black Sea (-65 (± 5)‰, ref. 8) one can calculate the approximate effect of methane formation on ΣCO_2 and $\delta^{13}C$. For organic carbon oxidized in the deep water $\delta^{13}C \simeq -22‰$, identical to the organic carbon in the surface sediment. This agreement between the ^{13}C contents of oxidized and sedimentary carbon suggests that there is no significant overall isotope fractionation during anaerobic oxidation. It is possible, however, that anaerobic oxidation preferentially affects a different set of organic components from those affected by aerobic oxidation and that this difference is at least partly responsible for the difference between the isotopic composition of the CO_2 added in the near-surface water and that added in the anoxic deep water.

The low $\delta^{13}C$ values of the sedimentary organic matter and of the organic carbon oxidized anaerobically can also be

Table 1 Range of Quantities Entering Calculation of Residence Time of Deep Water in Cariaco Trench

Quantity	Minimum	Maximum	Units	Remarks
Excess CO_2 in deep water	0.07	0.11	mmol kg^{-1}	Below interface and sill depth
Total oxidized organic C	840	1,320	g m^{-2}	Integrated over 1,000 m
Primary production	90	250	g C m^{-2} yr^{-1}	Refs. 1, 12, 13
Flux to deep water	4.5	50	g C m^{-2} yr^{-1}	5% and 20% of primary production[11]
Addition from continent	0	25	g C m^{-2} yr^{-1}	0 and half of flux to deep water (^{13}C data)
Oxidation in deep water	2.3	38	g C m^{-2} yr^{-1}	Half of total input to deep water[11]
Residence time	22	570	yr	Geometric mean: 112 yr

explained as being due to a contribution of continental organic matter to the sediment in the Cariaco Trench. Land plants are depleted in ^{13}C relative to marine plants[9] and the location of the trench is such that a contribution of sediment from land is to be expected. One of the cores taken on the recent cruise penetrated a tree trunk, 24 cm in diameter and buried just over 0.5 m; wood from the centre of the trunk had a ^{14}C age of $5,400 \pm 100$ yr and δ^{13}C of $-26.9\%_0$. Assuming a δ^{13}C of -26 to $-27\%_0$ for organic matter from land[10], I calculate that the continental contribution to the sedimentary organic matter in the trench may be as high as one-third, while the marine contribution is two-thirds or more.

The amount of oxidized organic carbon which has accumulated in the deep water is 0.07 mmol kg^{-1} relative to the water at the O_2-H_2S interface and 0.11 mmol kg^{-1} relative to sill depth (Fig. 1). To estimate the residence time of the deep water one needs, in principle, only to divide the total accumulation by the oxidation rate. In practice, the oxidation rate cannot be assessed very precisely. But by using available figures of the primary productivity of the area and drawing some analogies to the situation in the Black Sea, I have set limits on the oxidation rate which are unlikely to be exceeded (Table 1). Both extremes for the residence time should be regarded as highly unlikely because they incorporate successive minimization and maximization, respectively, at each step in the calculation. The likeliest value should lie near the geometric mean of the extremes, ~ 100 yr.

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17α(H) Hopane identified in Oil Shale of the Green River Formation (Eocene) by Carbon-13 NMR

THE occurrence of steroid and terpenoid saturated hydrocarbons in organic sediments is well known and their geological significance has been established[1-4]. These steranes and terpanes represent the complete reduction of naturally occurring steroids or terpenoids to relatively stable fossil molecules which preserve intact the complete molecular skeleton and stereochemistry of their precursors. Steranes and terpanes, together with other "biological markers", provided convincing proof for the biological origin of petroleums, oil shales, and other organic matter in sediments all over the world.

During the investigation of ^{13}C NMR shifts and the structural correspondence of pentacyclic triterpenes we undertook a ^{13}C NMR study on one of the most abundant components of the hexane soluble fraction of oil shale bitumen of the Green River Formation. Gelpi et al. isolated and collected this compound

for the first time employing their fully automatic capillary preparative gas chromatography system[5].

The compound is probably identical with the one representing GC peak No. 20 in the chromatogram described by Henderson et al.[6], and possibly the same constituent was detected by Hills et al.[7] as gas liquid chromatography (GLC) peak G in Nigerian crude oil distillates. Its molecular composition was $C_{30}H_{52}$ and it was tentatively identified on the basis of combined gas chromatography/mass spectrometry (GC/MS) data as a pentacyclic triterpane, possibly belonging to the hopane family[6]. Comparative studies with authentic standards employing capillary column GLC and MS suggest that this compound is 17α(H) hopane, structure II[8,9]. Here we present a rigorous proof derived exclusively from ^{13}C NMR data for the structure and stereochemistry of that important triterpenoid fossil molecule.

I   II
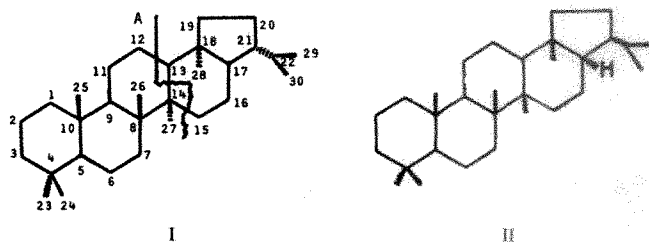
Using the preparative GLC technique and experimental conditions of Gelpi et al. (see Fig. 6D in ref. 5; thiourea non-adduct fraction) we collected 18.4 mg of white crystalline material of 97% purity (GC estimate). The substance melts at 155.5° C and is optically active; $[\alpha]_{20}^{D}$ is $+59.5$ in CHCl$_3$.

The ^{13}C NMR spectra were obtained on a Varian XL-100-15 CW spectrometer and decoupler, modified for Fourier transform spectroscopy with appropriate gating. A 1,000 W pulsed r.f. transmitter (Lawrence Berkeley Laboratory), 4-pole Butterworth filter, 15-bit analogue/digital converter, home-built computer interface and experimental controller, and 16 kwords of dedicated (32-bit word size) core memory, accessible to the rest of the 80 kwords of an XDS Sigma 7 computer for fast Fourier transform and 'CalComp' plot, complete the principal components of the system.

With the 16 k memory, the typical "computer resolution" for the normal range of ^{13}C chemical shifts has been 0.6 Hz or 0.025 p.p.m. entirely satisfactory for the intrinsic line width of compounds of polycyclic type, which is no better than 0.5 to 1.0 Hz under the experimental conditions (solvent, temperature, viscosity and so on). Also, for long signal averaging, the 32-bit word size avoids "wrap around" problems normally faced by computers with 16 to 20-bit word size. Chemical shift axes are plotted simultaneously with the spectra, giving high precision in shift measurements relative to an internal standard. Other subroutines have been developed to integrate line intensities, determine line widths, and perform other functions. Pulse decoupling[10] to avoid nuclear Overhauser intensity errors in intensity measurements has also been incorporated. A detailed discussion of operation and performance of on-line instrumentation will be published elsewhere.

The ^{13}C spectra of the collected unknown in both the proton noise decoupled mode and in the coherent off-resonance decoupled mode are shown in Fig. 1. As a rule, not one but several spectra were made in the off-resonance mode[11,12] to obtain identification from the splitting patterns caused by incomplete proton decoupling.

The line diagram (Fig. 1a) shows thirty ^{13}C resonances corresponding to thirty carbon atoms in the molecule. The chemical shift range of the resonances indicates complete saturation of all carbons present. The off-resonance spectra (Fig. 1b) revealed the chemical nature of these carbons—eight methyl groups and six methine, eleven methylene and five

Fig. 1 The natural abundance ^{13}C NMR spectra of the triterpane isolated from the bitumen of the oil shale of Green River Formation. *a*, Computer printout of the line diagram of the noise-decoupled spectrum. Resonance intensities are indicated by the height of the lines. *b*, Off-resonance spectrum. p, Primary; s, secondary; t, tertiary; q, quaternary carbons.

δ from CS_2 (p.p.m.)
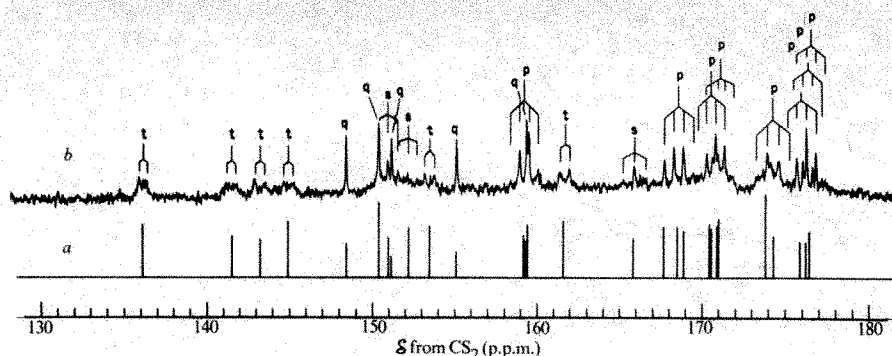
quaternary carbons were identified by examination of the splitting patterns. These carbons account for a molecular composition of $C_{30}H_{52}$ and suggest a pentacyclic triterpane. The presence of a five-membered ring is depicted by the number of quaternary carbon resonances (five) together with a tertiary resonance at 161.6 p.p.m. assigned to a methine carbon of an isopropyl group.

Comparisons within a series of pentacyclic triterpanes employing authentic hopane, moretane, lupane, and oleanane (B. B., P. C., D. M. W., and A. L. B., to be published) afforded further structural details. Two criteria were used in the comparison: (a) chemical shift agreement within 0.2 p.p.m.; (b) chemical identity of the resonances as derived from off-resonance data. It was found that the spectra of all five compounds contain an identical resonance pattern consisting of eighteen resonance lines, corresponding to eighteen identical carbon atoms. Considering the principle of structural additivity[13], it was concluded that the identical resonance pattern must represent an identical partial structure present in the analogues as well as in the unknown; for example the portion A in the structure of hopane (I). Detailed comparison with

hopane (I) which served henceforth as a "zero chemical shift" standard led to the completion of our structure elucidation (Fig. 2).

The close agreement of the quaternary resonance patterns (marked by asterisks) in both spectra suggests stereoisomeric relations between the two compounds, because methyl substitutions or skeletal changes usually result in far greater chemical shift distortions of bridgehead carbons in triterpenes.

The chemical shift pattern of the tertiary carbons needed detailed examinations. Seemingly, only one tertiary on C(17) has experienced a chemical shift of 15 p.p.m. upfield. This is a rather large distortion to be caused on one atom by steric interactions only, and the large shift probably represents a composite shift with the involvement of several tertiaries— C(17), C(13), and C(21)—but, by accidentally replacing each other, they lead to the degeneracy of the number of the observable chemical shifts. Owing to the close identity of the quaternary carbon patterns, the shifts of the tertiary carbons do have to stem from steric perturbations associated chiefly with through-space, possibly "γ-gauche", interactions[14].

Examination of methyl group positions quickly establishes

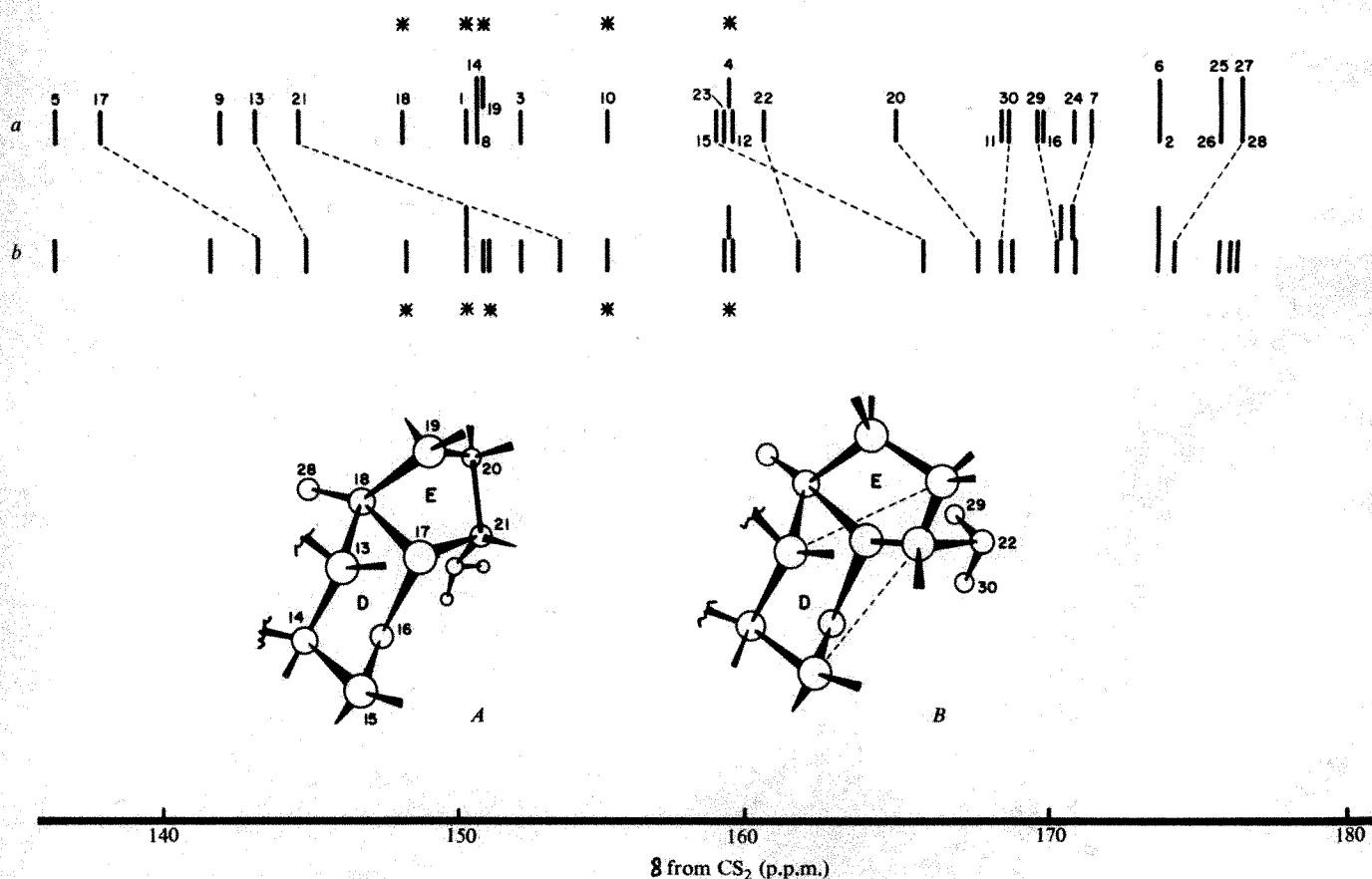δ from CS_2 (p.p.m.)

Fig. 2 ^{13}C chemical shift line diagram of (*a*) hopane, (*b*) unknown. Asterisks denote quaternary carbons; Dreiding models of D–E rings of (*A*) hopane and (*B*) 17α(H) hopane respectively.

that the role of axial methyls in these interactions is negligible. Methyls at C(23), (24), (25), (26), and (27) were not shifted at all; shifts involving the isopropyl group were readily assigned, and only C(28) exhibited a downfield shift of only 2.2 p.p.m. This leaves methylene-methine through-space interactions to account for the observed shifts of the tertiary carbons and, from the foregoing considerations, it is certain that the involved methylenes must be located in either D or E rings.

Such interactions can then only be affected by the inversion of the D–E ring junction which is *trans* in hopane (I) into a *cis* configuration resulting in several new γ-gauche interactions between tertiary and secondary ring carbons in 17α(H) hopane (II). Adapting structure II the shifts have been uniquely assigned as follows: C(21) is shifted 8.8 p.p.m. upfield because of two new buttressed γ-gauche involvements with C(15) and C(13); C(20) is shifted 2.6 p.p.m. associated with C(13); C(17) is shifted 5.2 p.p.m. upfield owing to its involvement in increased numbers of vicinal-gauche configurations. By cis-inversion of C(17), the C(28) methyl is bent away from D-ring carbons and the decreased steric perturbation resulted in a slight downfield shift (Fig. 2). This elucidation fully accounts for the variants of resonance pattern between the isolated triterpane and the selected analogue and is in rigorous accordance with the established rules of ¹³C NMR chemical shift. Further examination proved that none of the other twenty-four theoretically possible stereoisomers would correspond to the observed data. Thus, using the techniques of ¹³C NMR we have conclusively established the structure of the isolated triterpane to be 17α(H) hopane.

Table 1 ¹³C Chemical Shifts in p.p.m. from CS₂ and Assignments for the Spectra of Hopane and 17α(H) Hopane

Carbon	Hopane	17α(H) hopane
1	150.4	150.4
2	173.8	173.8
3	152.2	152.2
4	159.4	159.2
5	136.4	136.2
6	173.8	173.8
7	171.6	170.8
8	150.6	150.4
9	142.0	141.5
10	155.2	155.1
11	168.6	168.8
12	159.5	159.4
13	143.2	144.8
14	150.8	151.1
15	158.9	165.8
16	169.9	170.5
17	137.9	143.2
18	148.2	148.2
19	150.9	150.9
20	164.9	167.7
21	144.6	153.4
22	160.5	161.6
23	159.2	159.1
24	171.0	171.0
25	176.0	175.9
26	175.9	176.2
27	166.7	176.4
28	176.8	174.3
29	169.7	170.4
30	168.7	168.6

¹³C chemical shifts and assignments for the spectra of hopane and 17α(H) hopane are compiled in Table 1.

We thank Miss Patricia Wszolek and Dr Emilio Gelpi for the isolation of the triterpane. This work was supported by the National Aeronautics and Space Administration.

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Can Polyelectrolytes be called Catalysts?

IT is now well established that interionic reactions can be extensively enhanced[1,2] or retarded[3,4] by addition of polyelectrolytes, but whether the forward or reverse reaction is affected by polyelectrolytes is unknown. Here we report a kinetic investigation of an addition reaction of CN^- to a nicotinamide derivative — N-2'-(9-ethyladeninyl)-3-carbamoyl pyridinium chloride (NAA) (I), synthesized in this laboratory[5] in the presence and absence of polyelectrolyte. A similar reaction of nicotinamides quaternized with alkyl groups was also thoroughly investigated[6,7].

(I)   (II)
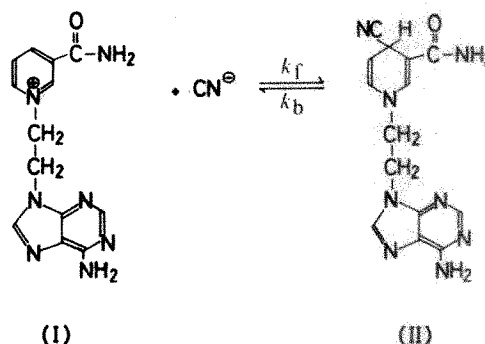
The second-order rate constant of the forward reaction k_f was determined by the stopped-flow technique using a Hitachi spectrophotometer model RSP-2. The temperature was 25° C. The appearance of II was followed at 340 nm. The equilibrium constant $K (= k_f/k_b)$ was obtained from the equilibrium optical density using the method of Cordes[8].

As in the ammonium cyanate-urea conversion[4], a reaction between unlike charged ionic species, reaction (1) was retarded by the addition of sodium polystyrenesulphonate (NaPSt). In other words the ratio k_f/k_0 (k_{f_0} is the rate constant without polyelectrolyte) was smaller than unity. Furthermore the effect of the polyelectrolyte on the equilibrium constant, K/K_0 (where K_0 is the equilibrium constant without polyelectrolyte), was also smaller than unity. At an NaPSt concentration of 2 mE l.⁻¹ both k_f/k_{f_0} and K/K_0 were 0.5. These ratios decreased with increasing concentration in the same proportion.

The effect of polyelectrolyte on the elementary processes can be discussed in terms of the free energies (Table 1). By polyelectrolyte addition $\Delta G \ddagger$ and ΔG were increased, which

Table 1 Thermodynamic Data of the NAA-CN⁻ Reaction with and without Polystyrenesulphonate (25° C)

[NaPSt] (E l.⁻¹)	$\Delta G\ddagger$ (kcalorie mol⁻¹)	ΔG (kcalorie mol⁻¹)	$\Delta G\ddagger-\Delta G$ (kcalorie mol⁻¹)
0	17.5	−3.1	20.6
2×10^{-3}	18.0	−2.6	20.6

$\Delta G\ddagger$, standard free energy of activation; ΔG, free energy of reaction.

is in agreement with the observed changes (mentioned above) of k_f and K. It should be mentioned that the value of ($\Delta G\ddagger$ $-\Delta G$) was 20.6 kcalories mol⁻¹ with and without the polyelectrolyte. The same value was also found for sodium polyethylene sulphonate and a diethyldiallylammonium chloride-SO_2 copolymer. These results show that the forward reaction was retarded whereas the backward reaction was not affected at all, and it was the initial state (neither the activated nor the final state) that was influenced by polyelectrolyte addition, in the reaction under consideration.

Our work suggests that polyelectrolytes should not be regarded as true catalysts according to the definition of Ostwald[9], who claimed that a catalyst must influence the forward and reverse reaction rates in the same proportion. Thus the term "polyelectrolyte catalysis" (or "polymer catalysis" in general), which is becoming popular, should be avoided.

Centeno et al.[10] have observed that addition of cyanide ion to N-hexadecyl 3-carbamoyl pyridinium ion was enhanced by a factor of 10^3 by hexadecyltrimethyl ammonium bromides and the association equilibrium constant was increased by a factor of about 2.5×10^4. This means that the backward reaction was retarded by a factor of 25. This observation apparently contradicts our results, but can be explained in terms of the hydrophobic interaction which is much greater than the repulsive forces between the positive charges of the surfactant and the substrate. Although the reason for the deceleration of the reverse reaction is not clear, we note that the forward and reverse reactions were influenced at different rates. Thus micelles are not catalysts either.

This work was supported by the Japanese Ministry of Education.

Note added in proof. It should be mentioned that the micellar influence on rate and equilibrium constant was reported earlier by Cordes et al.[11] and Fendler et al.[12,13]. In these studies, the rate and the equilibrium constant were shown to be affected in a different proportion, as was the case for systems mentioned in the text.

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Second Law of Thermodynamics

McCLARE[1] has proposed a complicated new statement of the Second Law of Thermodynamics. I wish to propose the following simple one:

"The only processes that can happen spontaneously are those that can in principle be made to yield work, for example, to lift up a weight."

Although I know of nearly a dozen statements of this Law which distinguish with varying degrees of clarity and universality those processes that can happen spontaneously from those that cannot, I have not come across the statement proposed except in the restricted field of mechanics: perhaps something similar is implied in a footnote by Everett[2].

A few examples of natural spontaneous processes will illustrate what is intended. Heat can flow only from a higher temperature to a lower, and if the flow takes place through a heat engine (for example, a thermojunction) part of the heat is converted into work. Diffusion of solutes occurs only from a high concentration to a lower one and this may be made to yield work by an arrangement of selective membranes (a van't Hoff box): should the solutes be electrically charged the arrangement can yield electrical work; this occurs during an action potential. Finally, it is well known that a chemical system subject to constant external pressure and under isothermal conditions, with negligible temperature gradients within itself, and at the same temperature T_e as its environment, will tend to react until its Gibbs's free energy is a minimum. This means that the reaction tends to continue spontaneously while the system is capable of performing work (by muscle, galvanic cell or van't Hoff box) and the reaction stops when it can no longer yield work.

A wide variety of examples could be given, and I have not come across any contrary ones: but it could be argued that it is impossible to prove a general case from particular examples, no matter how numerous. The general proof that follows is based on the fact that the creation of entropy is related in a simple fashion to the capacity for performing work.

One of the best, because most general, of the conventional statements of the Second Law is that the only processes that can happen spontaneously are those in which the entropy of the Universe is increased. The amount of entropy created, ΔS_{cr}, is thus positive for spontaneous processes and approaches zero as reversible equilibrium is approached. It can be shown that for any change of thermodynamic state, including changes of temperature, of a non-isolated system in an environment at temperature T_e there corresponds a certain maximum work performance, w_{max}, where $w_{max} = -\Delta U + T_e\Delta s$. If the work actually obtained is w it can be shown that the entropy created is

$$\Delta S_{cr} = (w_{max} - w)/T_e$$

Clearly w must take a value between zero and w_{max}; accordingly ΔS_{cr} must always be positive and it will have its greatest value when no external work is done. This argument can be easily extended to an isolated system: in that case the work resulting from the spontaneous change must be stored as such within the system. Thus the accepted criterion for spontaneity, that $\Delta S_{cr} > 0$, is the same as the proposed criterion that the system be capable of performing work.

Is anything gained by yet another addition to the anthology of statements of the Second Law? I believe that it is illuminating to see that the arcane world of thermodynamics is so similar to the everyday world of mechanics: and I think that many scientists find the concept of work simpler to understand and to manipulate correctly than the concept of entropy. For biologists in particular, who are continually concerned with systems that actually perform large amounts of mechanical electrical and osmotic work, I hope that my proposal represents a clarification.

I am not convinced that McClare really needs to put forward a new statement of the Second Law to support his principal

argument[1] that work corresponding to the free energy change of ATP splitting must somehow be stored as work if it is later to produce mechanical effect, and that if it becomes converted into heat it will for this purpose be lost. The Kelvin statement of the Second Law suffices to support this argument by showing that it is impossible to convert heat back into work in an isothermal system. I am not competent to judge the feasibility of McClare's detailed proposals for the mechanism of this work storage but would point to the increasing experimental evidence[4] that work is somehow stored in the crossbridges of muscle for many seconds, perhaps much longer; if his proposals will not do, others must be found. Finally, I would plead for more thought to be given to the problems that arise when the traditionally macroscopic arguments of thermodynamics must be applied to very small systems which, as McClare says, "use . . . one molecule of ATP at a time". It is far from clear[3] whether we must modify our basic ideas or not.

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Fig. 2 Stereoscan photomicrograph of breeding gallery of *H. rufipes* in the bark of RR 11, showing mature and developing perithecia of *C. ulmi* surrounded by mycelium, and spore slime from neaby coremia.

BIOLOGICAL SCIENCES

Origin of the Dutch Elm Disease Epidemic in Britain

WE have shown that two culturally distinguishable groups of *Ceratocystis ulmi* are present in Britain, one "fluffy" and aggressive, the other "waxy" and non-aggressive, and have presented evidence that the former is responsible for the current epidemic of Dutch elm disease[1]. It is of obvious interest to consider the origin of the aggressive strain.

There seem to be two chief alternatives: either that the aggressive strain arose by genetic change within an endemic non-aggressive gene pool, or that it was introduced to Britain. The separation of *C. ulmi* into two groups, apparently without a range of intermediates[1], can be reconciled with either alternative if we assume a rapid clonal build-up of the aggressive strain within the *C. ulmi* population once it had appeared.
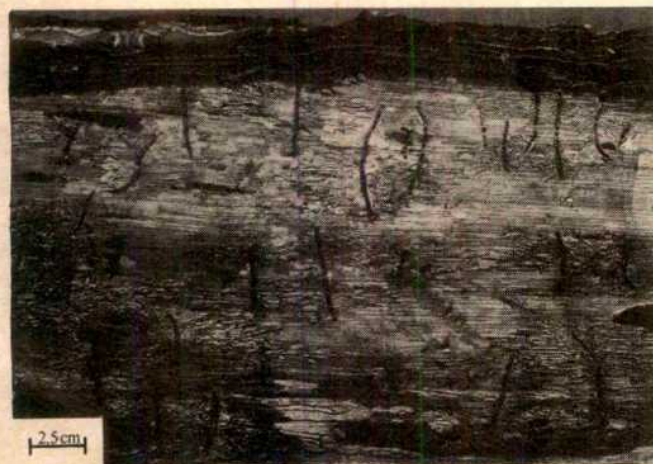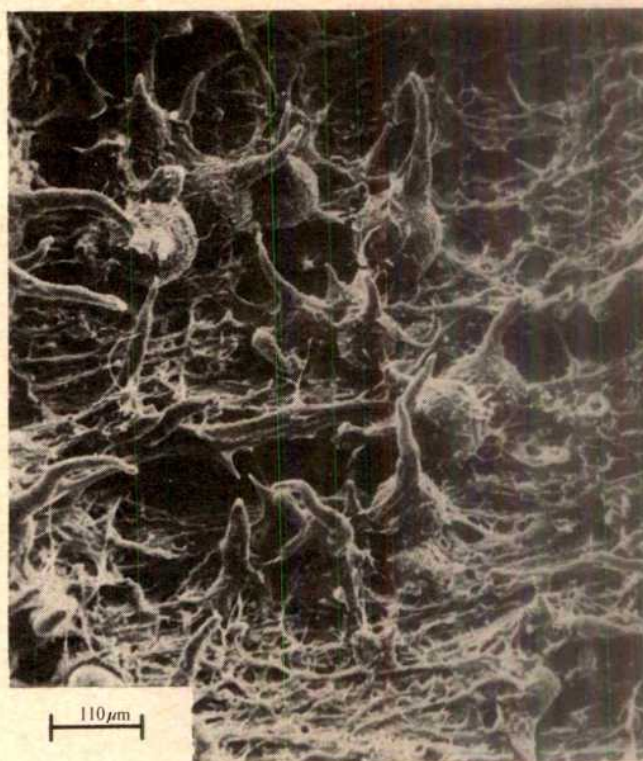
The close morphological and pathological similarity between the British aggressive and some North American isolates[1] suggests introduction, but can be reconciled with the theory of genetic change if a functional relationship exists between fluffy culture-type and aggressiveness.

Data from disease distribution are also inconclusive. Early Forestry Commission records indicate that the epidemic became evident in simultaneous outbreaks of severe disease in two widely separated areas, North Gloucestershire and South Essex, between 1965 and 1967. Although a similar genetic change in both areas during the same period seems unlikely, the records are too imprecise to preclude the possibility of material from a single disease origin being transported to the other. The introduction alternative seems more plausible for such widely spaced outbreaks of disease. These considerations have now been supplemented by strong evidence in favour of introduction.

In January 1973, we examined at Southampton Docks two 40 foot containers of Rock elm logs (*Ulmus thomasii*), recently imported from Toronto. The logs, up to about 35 foot long and 2 foot in diameter, were fresh and with the bark attached. Examination revealed that of the twenty logs, seven showed staining of doubtful cause in the bark and wood, and two others

Fig. 1 Sample of bark from Rock elm log RR 11, showing breeding galleries of *H. rufipes*.

Table 1 Comparison of Growth Rates of Waxy, Fluffy Aggressive and Rock Elm Isolates of *C. ulmi*

| Moreton waxy isolates | Fluffy isolates | | | Rock elm isolates |
	Tewkesbury	Essex	Chichester	
(M3) 2.65	(T14) 3.90	(O26) 3.78	(C19) 4.13	(RR 2) 3.78
(M5) 2.35	(T25) 3.68	(O29) 3.48	(C33) 3.40	(RR 7) 3.70
(M6) 2.40	(T39) 3.83	(O39) 3.58	(C37) 3.78	(RR 10) 3.60
(M8) 2.40	(T44) 3.55	(O42) 3.65	(C46) 3.70	(RR 11) 3.65
Mean 2.45	3.74	3.62	3.75	3.68

Isolate numbers in parentheses. Data for individual isolates are means of two replicates after 5 days growth on 20 ml. of 2% 'Oxoid Malt Extract Agar' at 18° C.
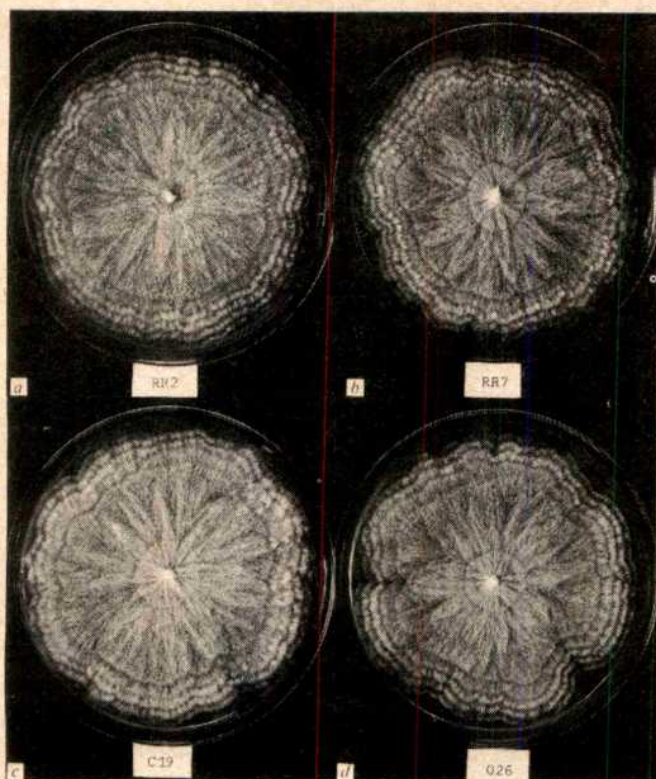
Fig. 3 Comparison of cultures of Rock elm and British aggressive isolates of *C. ulmi* on 2% 'Oxoid Malt Extract Agar' after 1 week in darkness at 18° C, followed by exposure to light. *a, b*, Rock elm isolates RR 2 and RR 7 respectively; *c, d*, British aggressive isolates C19 and O26 respectively. (See also Table 1.)

(RR 10 and RR 11) showed the distinct streaking in the outermost xylem vessels characteristic of Dutch elm disease. Samples were taken from four logs, including RR 10 and RR 11, and from each *C. ulmi* was isolated. In RR 10 and RR 11 extensive colonization of the inner bark by *C. ulmi* had occurred, and swards of coremia (asexual fruiting bodies) and mycelium were found in fissures between the inner and outer bark. In the bark, breeding galleries (Fig. 1), live adults, eggs and larvae of *Hylurgopinus rufipes*, a North American vector of Dutch elm disease, were found in quantity. The breeding galleries in one

log (RR 10) were packed with sticky coremial spore masses of *C. ulmi*. In the breeding galleries of RR 11 we found not only coremia but also abundant perithecia, the sexual stage of *C. ulmi* (Fig. 2). Many perithecia were exuding ascospores which on culturing were found to be viable.

When the isolates of *C. ulmi* obtained from each of the four sample logs were compared with twelve British aggressive isolates (four from each of the three main outbreak areas[1]) and four non-aggressive isolates from Moreton in Oxfordshire, they fell into the fluffy group on the basis of growth rate (Table 1) and culture morphology (Fig. 3). It was evident that *C. ulmi* from the Canadian elm logs closely resembled the aggressive strain of the fungus present in this country.

Rock elm is a North American species found chiefly in the Great Lakes region[2], its distribution in Canada being confined to south-east Ontario (Fig. 4). As its name implies, it produces an extremely hard timber, which is much favoured on account of its straight grain, great density and strength. It seems that for about one hundred years Rock elm logs with bark attached have been imported into Britain from Canada, principally for boat building. Dutch elm disease entered the Toronto region from the United States by way of Windsor and the Niagara peninsula in 1950 (ref. 3). By the early 1960s the disease was present throughout south-east Ontario, and the importation into Britain of the disease on logs of Rock elm from any point in the range of this species in Canada was a possibility. *Hylurgopinus rufipes* is present throughout southern Ontario (Fig. 4) and the small European bark beetle *Scolytus multistriatus* is also present, with a range similar to that of Rock elm[4].

Investigation of the trade has shown that the chief ports of entry into England during the 1960s were Avonmouth, Liverpool, London and Southampton, and among the chief centres of usage were Chatham, Plymouth and Portsmouth. At that time the logs were not in containers, but were carried as deck or loose cargo. From May to September bark beetles, whether *H. rufipes* or *S. multistriatus* carrying spores of *C. ulmi*, could be expected to emerge from infested logs similar to those we examined, either at the docks or in transit to boat and timber yards. They would then tend to migrate to adjacent healthy elms for maturation feeding, thus initiating infection. It is further possible that logs arriving in this country could have afforded breeding material for native *Scolytus* species which could then have picked up the Canadian strains of the fungus. Once introduced into our native elms, the aggressive strain
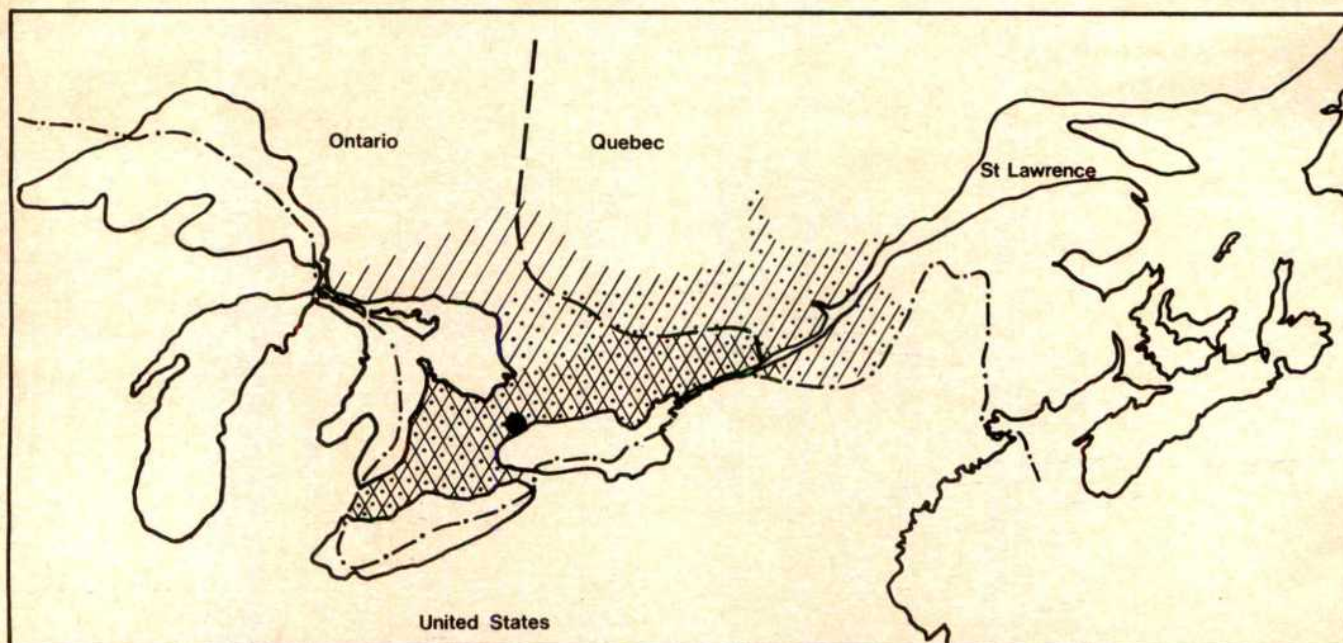

Fig. 4 Distribution of Rock elm (*Ulmus thomasii*, ▧) in Canada, together with the distribution of *Hylurgopinus rufipes* (▨) and Dutch elm disease (▦) in the Toronto (●) area in 1963. (Adapted from refs. 2, 3 and 4.)
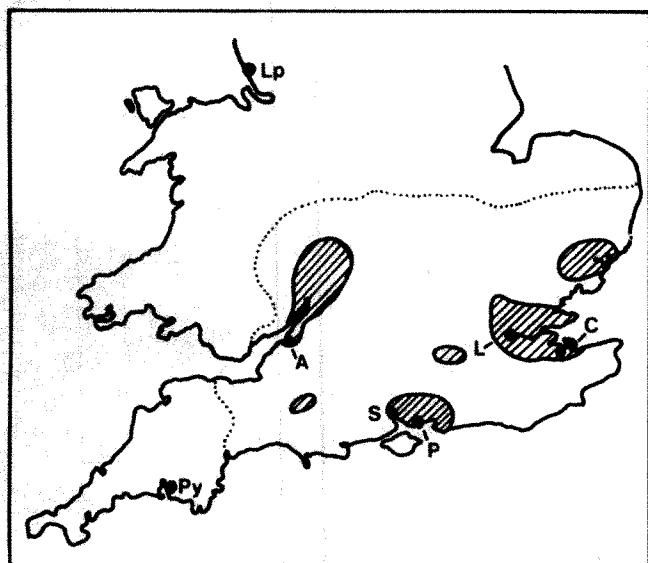
Fig. 5 Map of southern Britain showing the relationship between the chief areas of Dutch elm disease identified in the 1971 survey, and ports of entry and centres of usage of Rock elm. . . . , Principal area covered by survey; ▨, areas worst affected by disease; A, Avonmouth; C, Chatham; L, London; Lp, Liverpool; P, Portsmouth; Py, Plymouth; S, Southampton.

would, by its lethal nature, increase the locally available beetle breeding material. This in turn would result in rapid development of the disease outbreaks to epidemic proportions.

The ports and centres of usage mentioned above and the principal disease areas identified in the 1971 Forestry Commission Survey of southern England[5] are shown in Fig. 5. It seems that disease in two of these areas, namely that on the south coast and that around the Thames Estuary, could well be associated directly with sites of importation and usage. Other disease centres such as that in the Severn Vale could have originated during the transport of imported logs by road or rail to sites where they were to be cut. In the past few years new disease centres have almost certainly arisen as a result of the transport of infected native elm material into regions previously free from the aggressive strain.

We conclude that the current epidemic of Dutch elm disease has most probably resulted from the importation of diseased elm logs carrying aggressive North American strains of C. ulmi. It therefore seems that two the distinct groups of C. ulmi identified by sampling in 1972 (ref. 1) represented elements of two populations hitherto geographically isolated: one aggressive, originating from within the North American population, and probably responsible for the continued activity of the disease on that continent; the other non-aggressive, representing the residual population from the previous British epidemic, following its decline during the 1930s (ref. 6).

As perithecia of C. ulmi were present on the logs we examined it is apparent that this process of introduction could have resulted in the entry of a range of genetic material, including the two compatibility types. Our preliminary data (unpublished) indicate that both compatibility types are also present among British non-aggressive isolates. There is thus the possibility of outcrossing between the two groups, aggressive and non-aggressive, in nature and hence of the appearance of intermediate phenotypes. We are considering the implications of these findings for our present work on the population dynamics of C. ulmi and on the genetic control of pathogenicity.

Movement of elm logs has played an important part in the history of Dutch elm disease, as C. ulmi and Scolytus multistriatus reached the United States from Europe on elm burl logs imported for the manufacture of veneer[7]. It appears that the same means has now caused a resurgence of the disease in Britain. This event not only emphasizes the continuing danger, stressed by Peace[8], of the introduction into Britain of

serious tree diseases not now present such as oak wilt (Ceratocystic fagacearum), chestnut blight (Endothia parasitica) and elm phloem necrosis, but also demonstrates the serious danger of introducing new and more aggressive strains of tree pathogens already present.

We thank Chris Walker of our Entomology Section for identifying and assisting with collection of material of Hylurgopinus rufipes. We also thank Miss Jenny Cross and Miss Polly Smith for technical assistance, and Mrs Hazel Geoffrey and John Williams for the preparation of photographs and diagrams.

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Evidence for a Tumour-associated Antigen in Human Malignant Melanoma

TUMOUR-directed antibodies are found in the serum of patients suffering from malignant melanoma[1-5], and so we have attempted to detect tumour-associated antigens in extracts from melanoma tumours and urine of patients.

Preliminary experiments showed that after immunization of rabbits with concentrated dialysed urine of melanoma patients, antisera were obtained which, after absorption, reacted in the double diffusion[6] or single radial diffusion[7] test which concentrated urine samples from other melanoma patients, but failed to react with urine samples of normal individuals or patients without neuroectodermal neoplasia. Animals immunized with melanoma extracts produced antisera which after absorption showed identical antibody specificity.

These antisera were prepared by immunizing rabbits at 8 days intervals with two injections of 2 mg of crude antigen in Freund's complete adjuvant in the two hind-food pads. Each injection consisted of 1.2 ml. of material prepared by mixing 0.6 ml. adjuvant with an equal volume of concentrated dialysed urine or with an equal volume of a Tris-saline extract of a melanoma tumour. Blood was withdrawn 28 days from the start of immunization. The resulting antisera were absorbed with lyophilized normal human plasma, normal human urine, Tris-saline extracts of normal skin and ABO red cell stromata.

The specific antigenic activities of the melanoma urine and of the tumour extracts were then isolated by several chromatographic procedures and by different preparative electrophoreses as follows. The presence of antigenic activity at each stage of the following purification was determined by double diffusion against several specific antisera, prepared as described above.

Tumour tissue was homogenized at 30,000 r.p.m. and 50,000 Hz. Extraction was performed with an equal volume of 0.1 M Tris NaCl buffer, pH 7.5, and the supernatant was lyophilized after centrifugation of the homogenate at 1,500g for 30 min and 20,000g for 60 min. Double diffusion analysis revealed the presence of melanoma activity in this material. An aliquot of 2 g of the lyophilized Tris-saline extract was dissolved in 3 ml. of 0.2 M ammonia and applied to a 'Sephadex G-10' column equilibrated with the same solvent. The first peak was

collected and lyophilized as it contained the whole melanoma activity. A further fractionation of this material on 'Sephadex G-100' eliminated, in the exclusion peak, all the contaminating immunoglobulins and other macromolecules. The melanoma activity was located in the second peak which was collected and lyophilized. This material was then separated into 4 peaks on a 'Sephadex G-75' column, and the melanoma activity located in peaks 1 and 2, which were collected. Immunoelectrophoretic analyses revealed that the main contaminant remaining in this material was albumin, eliminated by Pevikon electrophoresis[8] under standard conditions (0.01 M veronal buffer, pH 8.6) on a block 4.5 × 20 × 1 cm. After electrophoresis at 115 V and 7 mA for 15 h, the block was cut into fractions of 1 cm, and the melanoma activity located between 9 and 11 cm from the origin, while most of the albumin was at 15 cm from the origin. Finally, Pevikon fractions containing melanoma activity were applied on a 110 ml. electrofocusing column in a sucrose density gradient using a pH range from 3 to 6. Focusing was achieved by electrophoresis at 300 V and 72 h and the fractions containing melanoma activity were located between pH 4.5 and 5.5.

Lyophilized urine samples from melanoma patients were fractionated according to the same purification scheme as described above for tumour extracts, with the only exception that the 'G-100' purification step was omitted. Melanoma activity was also recovered in the fractions between pH 4.5 and 5.5 in the electrofocusing purification step.

Antisera were prepared against these active materials isolated by electrofocusing, from the tumour and the urine of melanoma patients. The antisera did not have to be absorbed as described above. A line of identity was demonstrated, using these antisera in the double diffusion test against different melanoma urine samples. This indicates that all materials used for immunization, even with different isoelectric points, contain the same antigenic determinants. Moreover, they must be of similar sizes because they were not separated by gel filtration and block electrophoresis. Preliminary molecular weight determinations by polyacrylamide gel electrophoresis[9] showed that these antigen(s) have molecular weights between 40,000 and 60,000 and would therefore display beta mobility in Pevikon electrophoresis. It is not clear what the differences are between these similar or identical antigens. Gel electrofocusing[10-12] experiments on antigens purified by preparative electrofocusing showed that these antigens are very rapidly degraded.

All antisera produced were screened against a large panel of different concentrated urine samples. Twenty-nine out of thirty-two samples from melanoma patients reacted positively (Table 1), while sixty-nine out of seventy-two control urine samples gave negative reactions. The three "non-melanoma" urine samples with positive reactions were collected from two patients with neuroblastoma and from a patient with ganglioneuroma. Positive melanoma urine samples were collected

Table 1 Results of Screening Urine Samples with Rabbit Anti-Melanoma Antiserum

Source of urine samples	Total No. of patients	Reaction in double diffusion against anti-melanoma antiserum Positive (+)	Negative (−)
Melanoma	32	29	3
Carcinoma	20	0	20
Myeloma	7	0	7
Other tumours *	8	3 †	5
Various non-malignant diseases	24	0	24
Nephropathy	4	0	4
Healthy control	9	0	9
Total "non-melanoma"	72	3	69

* 2 Sarcomas, 1 Wilms's tumour, 2 neuroblastomas, 1 ganglioneuroma, 2 phaeochromocytomas.
† 2 Neuroblastomas, 1 ganglioneuroma.

Table 2 Number of Positive Melanoma Urine Samples of Different Stages of the Disease

Type of tumour	Total No. of patients	Positive reaction against anti-melanoma antiserum (+)
Primary melanotic *	13	12
Primary amelanotic *	1	1
General melanotic †	17	15
General amelanotic †	1	1

* Malignant melanomas confined to primary anatomical site.
† Malignant melanomas spread beyond the regional lymph nodes.

from individuals with melanotic or amelanotic tumours (Table 2) in all three stages of the disease described by Lewis et al.[2].

Our experiments, so far, indicate the presence of a common antigen in the tumour which is excreted in the patients' urine. However, the question remains as to whether these tumour-associated antigen(s) are tissue-specific or tumour-specific. It is also unknown whether the common tumour associated antigen(s) of melanomas are of embryonic or viral type. A possible embryonic origin, however, is suggested by the fact that the three positive "non-melanoma" urine samples were from two neuroblastomas and one ganglioneuroma. The precursor cells of all three of these tumours are thought to originate in the neural tube.

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6-Azauridine-5′-phosphoric Acid: Unusual Molecular Structure and Functional Mechanism

6-AZAURIDINE has been used successfully in the treatment of leukaemia[1]. The nucleoside is not effective as such but is converted *in vivo* by the enzyme uridine kinase to 6-azauridine-5′-phosphate, which inhibits the enzyme orotidylic acid decarboxylase[2-4]. This inhibition stops the metabolism of orotidine-5′-phosphate to uridine-5′-phosphate, that is the *de novo* synthesis of uridylic acid (Fig. 1).

In crystalline state and in solution, 6-azauridine occurs in the *anti* conformation with the ribose moiety in the C(3′)-*endo* envelope form and the conformation about the C(4′)–C(5′) bond is not the usual *gauche, gauche* with atom O(5′) positioned above the ribose ring but rather the *gauche, trans* form[5,6]
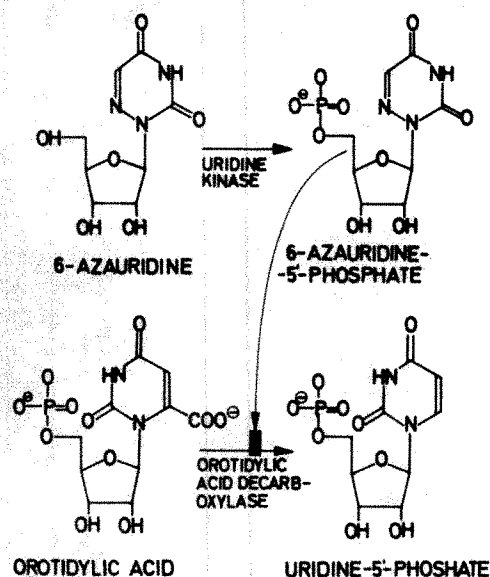
Fig. 1 Mechanism of inhibition of orotidylic acid decarboxylase by 6-azauridine.

(Fig. 2). Our X-ray study on 6-azauridine-5'-phosphate was undertaken in order to establish whether it assumes a similar conformation as 6-azauridine or whether it occurs in the normal *gauche, gauche* form found for all the nucleotides investigated so far[7,8].
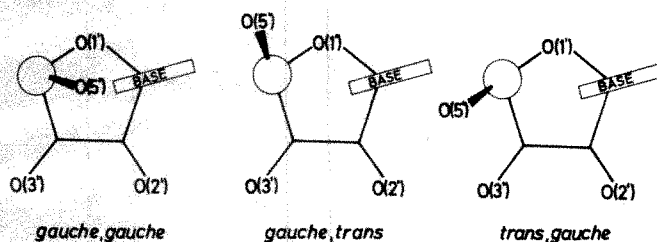

Fig. 2 Conformation about the nucleoside C(4')-C(5') bond.

6-Azauridine-5'-phosphoric acid was crystallized from iso-propanol/water as thin needles with orthorhombic lattice symmetry, space group $P2_12_12_1$ and cell constants $a=20.615$ Å, $b=6.265$ Å, $c=11.881$ Å. We concluded from a measurement of the crystal density that the asymmetric unit contained the trihydrate of 6-azauridine-5'-phosphoric acid. The structure was solved from diffractometer data by application of Patterson methods and refined by full matrix least squares methods to a crystallographic discrepancy index $R=7\%$. A difference Fourier synthesis computed at this stage revealed no serious discrepancies with the derived model.

Bond angles and distances within the 6-azauridine-5'-phosphoric acid molecules (Fig. 3) are comparable to those observed for 6-azauridine and for other nucleoside-5'-phosphates and will be discussed elsewhere, together with a full account of this structure. The location of the acid hydrogen ion is not obvious from the latest difference Fourier synthesis. Yet it is certain that the 6-azauracil moiety in 6-azauridine-5'-phosphoric acid is uncharged as its bond distances and angles are identical within experimental errors with the values found in 6-azauridine.

The conformation of 6-azauridine-5'-phosphoric acid about the glycosidic C(1')-N(1) linkage is *anti* with the torsional angle $C(2')-C(1')-N(1)-N(6) = -33°$ (that is, the $C(2) = O(2)$ keto group is pointing away from the ribose ring). The ribose moiety is in a rather symmetrical $C(2')$-*exo*, $C(3')$-*endo* half chair form. The conformation about the C(4')-C(5') bond is

not *gauche, gauche* as in all the nucleoside-5'-phosphates so far studied but rather *gauche, trans* as in 6-azauridine, with torsional angles $O(1')-C(4')-C(5')-O(5')$, 71°; and $C(3')-C(4')-C(5')-O(5')$, −172°.

To illustrate the change in molecular geometry caused by the change in conformation from *gauche, gauche* to *gauche, trans* we have depicted in Fig. 4 the X-ray results obtained for this structure and for uridine-5'-phosphate[9], which was found to occur in the *gauche, gauche* conformation. When the ribose atoms C(1'), O(1') and C(4') are placed in coincidence, the phosphorus atoms are separated by 4.25 Å.
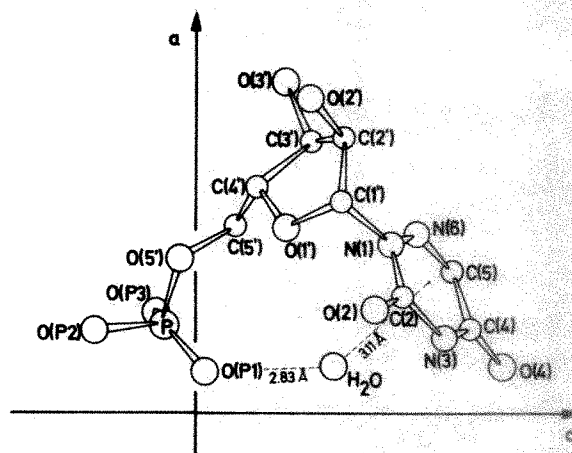

Fig. 3 The molecular structure of 6-azauridine-5'-phosphoric acid viewed down the b-axis. Two of the three water molecules within the asymmetric unit are omitted.

The two molecules shown in Fig. 4 are chemically different only in position 6 of the heterocyclic base. Extended Hückel calculations revealed that in 6-azauridine the N(6) atom accumulates a charge of −0.47 e, compared with a charge of +0.28 e at atom C(6) of uridine[10]. Thus, it appears that the *gauche, trans* conformation of 6-azauridine as well as of 6-azauridine-5'-phosphoric acid is due to an electrostatic repulsion between N(6) and O(5'). Furthermore, in 6-azauridine-5'-phosphoric acid the hydrogen bond interaction C(6)-H . . . O(5') discussed for uridine-5'-phosphate derivatives[11] cannot stabilize the *gauche, gauche* conformation.

As the structure of orotidylic acid has not yet been determined, the reason why 6-azauridine-5'-phosphate is an inhibitor for orotidylic acid decarboxylase must be derived by analogy. It is known that orotidine occurs in the *syn*-conformation due to the bulky carboxyl group at the base C(6) position[14,15] and exhibits, in solution, a *gauche, trans* or *trans, gauche* conforma-
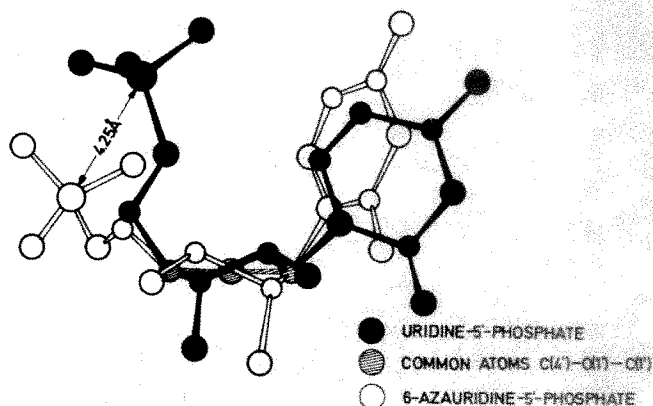

Fig. 4 Comparison of the *gauche, gauche* and *gauche, trans* structure of uridine-5'-phosphate and 6-azauridine-5'-phosphoric acid respectively.

tion about the C(4')–C(5') bond[14]. Furthermore, a *gauche, trans* conformation has been observed for a crystalline O(5') ester analogue in the *syn* conformation, 2'-deoxy-2'-fluorouridine-3',5'-diacetate (Fig. 5) (D. S., W. S., and P. Main, in preparation).
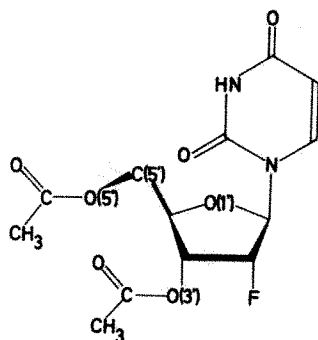
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Fig. 5 Chemical structure of 2'-deoxy-2'-fluorouridine-3',5'-diacetate.

Thus, one would expect orotidylic acid to occur in *syn* and *gauche, trans* conformations as well. This peculiar molecular structure would explain why 6-azauridine-5'-phosphate with similar *gauche, trans* orientation of the phosphate group acts as an inhibitor for orotidylic acid decarboxylase: the antimetabolite mimics the metabolite and is bonded to the active site of orotidylic acid decarboxylase. This also suggests why other pyrimidine nucleosides which are not substituted in the base 6-position do not act as inhibitors: they occur in normal *anti* and *gauche, gauche* conformations.

Another conclusion derived from this study concerns the enzyme uridine kinase. As both substrate and reaction product exhibit an unusual *gauche, trans* conformation, the enzyme is either not very specific, or it forces the substrate 6-azauridine during bonding at the surface of the active site to assume a "normal" *gauche, gauche* conformation like uridine.

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The Identification of Labelled Structures on Autoradiographs

THERE is no agreed method of deciding whether or not a given structure is radioactive from its autoradiograph. Some authors require that a cell, for instance, should have five or more overlying grains to be considered labelled, whereas others are satisfied with three or four grains. By setting such an arbitrary limit, the experimenter risks accepting as labelled some non-radioactive cells which, by chance, have a higher number of background grains over them, and risks rejecting as unlabelled those radioactive cells which have failed to give rise to the requisite number of grains over them. In an ideal preparation with very low background and high grain densities over radioactive structures, the error introduced by this arbitrary definition of labelling is likely to be small. The smaller the differences between the mean grain densities over background and over the radioactive sources, however, the greater this error becomes.

This problem has been recognized and solutions have been proposed in several previous publications[1-5]. These all tend to give similar values for the percentage of a given population of structures that is radioactive, when the grain densities over labelled sources are high, but at mean grain densities approaching background levels the values derived by these methods diverge considerably.

Here we present an analytical method which is simple and direct to use, and accurate even when some of the radioactive cells have no grains over them at all. We start from the assumption that grain densities over background areas and over radioactive sources both have a Poisson distribution. This assumption is generally valid[6], though exceptions do occur.

In order to make allowance for cells which produce no grains it is necessary to make more than one measurement of the radioactive cells, and to compare these with measurements made from similar areas of emulsion giving values for background: these may be from areas on the same autoradiographs away from the radioactive cells or non-radioactive cells autoradiographed under identical conditions, as appropriate. The two measurements we have chosen are the percentage of cells with one or more grains over them, and the mean number of grains per cell.

Having obtained the measurements, one then calculates A, B, and C as follows.

$A = 100 - (\%$ non-radioactive cells with one or more grains)

$B = (\%$ radioactive cells with one or more grains) $-$ ($\%$ non-radioactive cells with one or more grains)

$C = $ (mean number of grains per radioactive cell) $-$ (mean number of grains per non-radioactive cell)

The true percentage of labelled cells, D, is then given by

$$B/AC = D/100 \, C \, [1 - \exp(-100 \, C/D)]$$

Rather than solve this equation for each experimental result, Fig. 1 can be used. We first calculate B/AC and locate this value on the vertical scale, then read across to intersect with the curve, and finally down to the corresponding value on the horizontal scale, which gives $100 \, C/D$. We have already calculated C, so we can now evaluate D.

We have chosen an experiment to illustrate our method in which the random or background contribution to the observed grain densities was high, and the level of labelling over radioactive sources likely to be low. Rat thoracic duct lymphocytes were incubated with ^{125}I-labelled normal rabbit globulin,
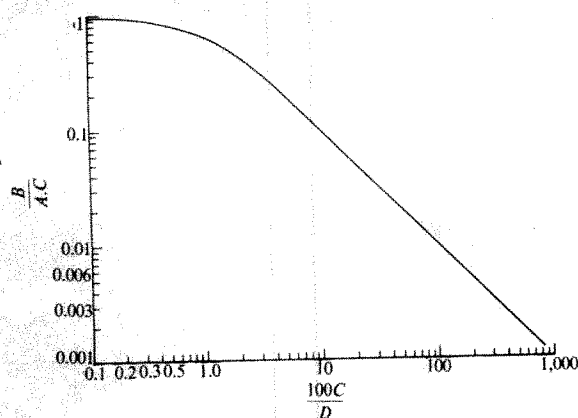
Fig. 1 Scale to determine the true percentage of labelled cells.

washed, centrifuged and resuspended three times in non-radioactive buffer, then smeared on slides and autoradiographed by dipping in Ilford G5 emulsion[7]. Background measured on areas of emulsion distant from cells on these slides was higher than on autoradiographs of non-radioactive suspensions, partly due to the presence of traces of ^{125}I in the suspending medium and partly to the gamma and X-ray components of the emission of ^{125}I. Our background areas were therefore taken from the experimental slides, away from underlying cells. Scintillation counting experiments revealed that on average each lymphocyte was producing one disintegration every 4 days. The experiment was designed to show if all lymphocytes in this sample were equally radioactive, or if a sub-group possessed the ability to bind immunologically non-specific globulins.
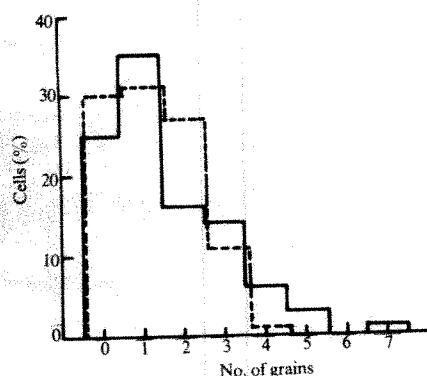

Fig. 2 Rat thoracic duct lymphocytes incubated with ^{125}I-labelled rabbit globulin. - - - -, Emulsion remote from labelled cells; ——, labelled cells.

The results are shown in Fig. 2: the grain counts over cells are low, mostly overlapping those from background areas. From our results $A = 100 - 70 = 30$, $B = 75 - 70 = 5$, $C = 1.55 - 1.22 = 0.33$ and $B/AC = 0.505$; from Fig. 1 this value of B/AC gives $100 \, C/D = 1.57$, so that knowing $C = 0.33$, $D = 21\%$.

This example shows that large numbers of cells may be labelled even though most of the cells have no grains or only one or two grains overlying them. It is important to emphasize that extensive counting must be performed. Calculating A, B and C involves calculating differences between observations, so that small errors in the observations can mean large errors in the differences. These errors can be minimized by keeping A, B and C as large as possible by using the most sensitive methods to detect the radioactivity in the labelled cells, and by ensuring that the background is low in the unlabelled areas. It is difficult to suggest a simple method of determining how many areas to count in any given experiment. If the experi-

mental and background distributions overlap, and a highly accurate final answer is needed, repeated sampling with 200 cells per experiment will generate data the reproducibility of which will indicate the total number of counts required.

This approach should avoid the necessity of setting up arbitrary definitions of a labelled cell. All such definitions introduce considerable errors by excluding labelled cells which either produce no grains or do not produce the requisite number of grains. Using our analytical procedure these problems are avoided, and a correction can be made for radioactive background without recourse to elaborate computer programs. The present correction approximates to Stillström's[4] when the cells are very radioactive.

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Microspectrophotometry of Trypsin-Leishman-stained Human Chromosomes

RECENTLY new chromosome banding techniques have become available, by means of which each chromosome in the human karyotype can be identified[1-3]. To illustrate graphically quinacrine (Q)-stained metaphase chromosomes, Caspersson et al. developed a technique using densitometric measurements from photographs[3]. Diagrams of differential fluorescence have been computerized, and a method for automatic karyotyping is being developed[4-6].

To measure the number, position, relative size and intensity of bands produced by stains other than Q, and to avoid photographs of the banding patterns, we have produced diagrams from trypsin-treated chromosomes stained with Leishman from specimen. Human metaphase chromosomes from lymphocytes[7] were stained with a modified trypsin-Leishman method[1].

Six suitable metaphase figures with chromosomes of different degree of contraction from four individuals were selected. The absorption pattern of each chromosome was registered by means of the microspectrophotometer UMSP-I (Zeiss) at a wavelength of 545 nm (absorption maximum, Leishman-stained regions). A measuring area with a diameter of 0.3 µm was selected, and light absorbance of this area in continuous steps down the midline of the chromosome was graphically or digitally recorded[8].
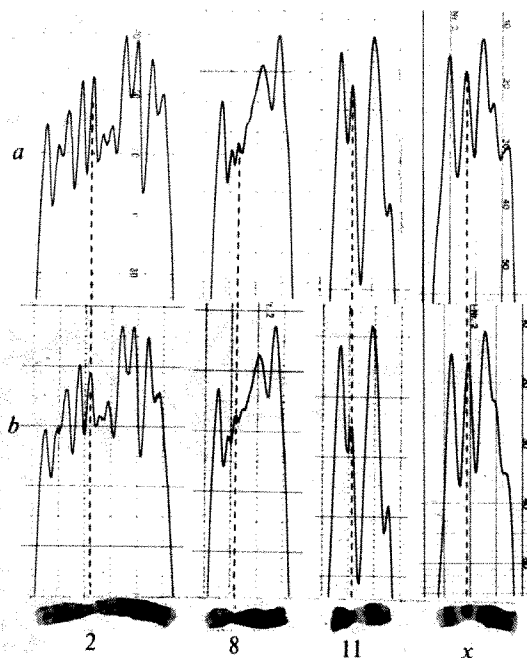

Fig. 1 Chromosomes 2, 8, 11 and *X*; corresponding diagrams were measured twice on different occasions to illustrate the reproducibility of the diagrams. All chromosomes are placed with the short arm to the left. – – –, Position of the centromere.

Each chromosome was measured four times, twice from one end and twice from the other end of the chromosome. Repeated measurements were performed at different times. The centromere position and the chromosome lengths were measured with a micrometer.

Fig. 1 shows the reproducibility of the banding patterns from four different chromosomes recorded directly from the slides. All information on the slide, here illustrated on photomicrographs, is found on the diagrams.

Both diagrams from, for example, chromosome No. 8 have three rather large spikes, all similar in size, position and shape and corresponding to the three dark bands on the photomicrograph. Three smaller but somewhat variable spikes around the centromere correspond to indistinct bands on the photomicrograph.

Chromosome 11 has a broad light band followed by a broad dark band on the long arm. These two bands correspond in both diagrams to a deep wave followed by a large spike.

On the *X* chromosome are two dark bands, one on each side of the centromere (here heavily stained), and further distally on the long arm are more indistinct bands. A large spike corresponding to each of the two dark bands, a spike corresponding to the dark centromere region and two small spikes which are more pronounced on (*a*) than on (*b*) are evident on the diagrams.

Fig. 2 shows diagrams of the same chromosome from four different metaphases. The photomicrographs show some variations between different chromosomes 1 (top) concerning contraction, number of bands and staining intensity. On 1 (*a*) and (*c*) two proximal dark bands on the short arm are

clearly illustrated on the corresponding diagrams. On 1 (*b*) the most proximal of the two dark bands is fairly indistinct, corresponding to a weakly visualized spike. On 1 (*d*) there is only one broad band in the proximal part of the short arm. This corresponds to a broad spike. The dark band on the proximal part of the long arm is on all diagrams. On the distal part of the long arm, depending on the degree of contraction, three or four dark bands are present, corresponding to the number of spikes on the diagrams.

Chromosome 7 (bottom) has three dark bands: one in the distal part of the short arm and two in the middle of the long arm. These bands correspond to large spikes on the diagrams. The proximal part of the short arm and the centromere region are variably stained; these features are illustrated as variable spikes.

Spikes and bands corresponded to each other with regard to position, size and shape; thus each chromosome had a characteristic diagram.

The difficulties in sweeping the measuring area exactly down the midline of the chromosome were responsible for the slight deficiencies in the reproducibility of the diagrams and these, together with differences in staining intensity and degree of contraction of the chromosomes, contributed to the variations of diagrams from homologous chromosomes and identical chromosomes from different metaphases. Further standardization of preparation and staining will probably improve matters.
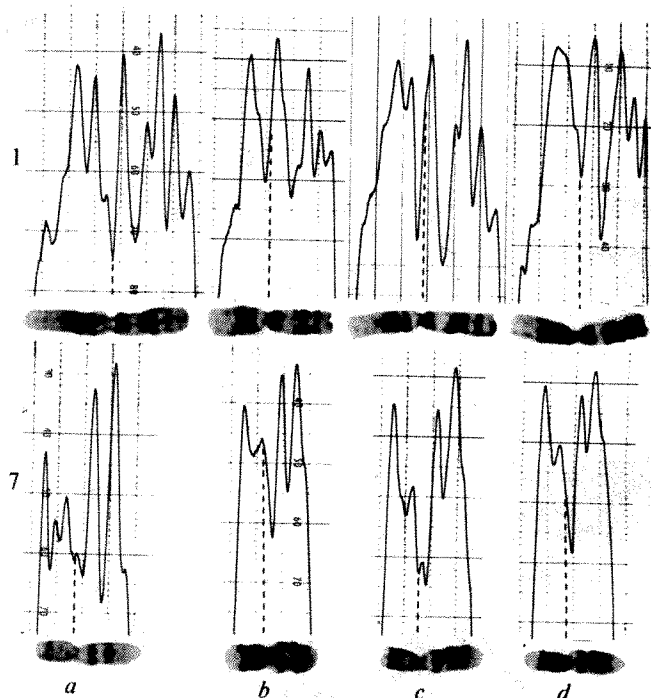

a   *b*   *c*   *d*

Fig. 2 Chromosomes 1 (top) and 7 (bottom) from four different metaphases with corresponding diagrams developed directly from the slide. Small variations in the diagrams are caused by corresponding variations in the banding patterns illustrated on the photomicrographs. Note the polymorphism of the darkly stained area on the long arm near the centromere on chromosome 1.

The UMSP used has a circular measuring area. Varying diameters from 0.3 to 1.0 µm showed that smaller areas give more detailed diagrams. As chromosomes are 1 to 2 µm wide only a portion of the whole chromosome is measured. TL-stained chromosomes often show banding across the whole chromosome, but variations occur, especially in light bands. By measuring only a fraction of a band, variation across the chromosome may lead to differences in absorption patterns.

A slit aperture 0.3×2.0 μm might give more constant diagrams[3].

The amount of stain bound varies with circumstances, so TL staining does not meet the requirements of stoichiometry. Further investigations are necessary. For identification, however, this is of secondary importance. The aim is to determine the location of stain maxima and minima. The position of the centromere on diagrams can be determined either directly in the microscope or on the photomicrographs. Methods for detecting the centromere by means of the instrument are being investigated. Curved chromosomes are divided into several parts with different axes. Microspectrophotometry has been used to establish a technique for accurate, objective, automatic recording of banding patterns of TL-stained metaphase chromosomes. Diagrams are constant and characteristic. Identification of chromosomes and diagnosis of the exact nature of abnormalities seem possible (ref. 9 and C. L., J. P. and S. Vestermark, unpublished).
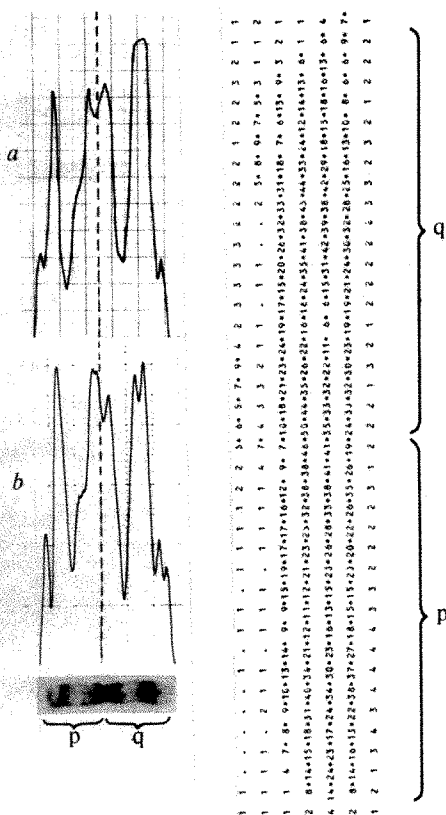

Fig. 3 Right: part of a digitally recorded metaphase (chromosome 3, p: short arm, and q: long arm); this chromosome has been converted manually to a diagram (*a*) by combining the figures along the longitudinal direction of the chromosome. *b*, The same chromosome illustrated graphically by the technique described in the text.

The technique could be very useful for performing comparative studies with other banding techniques. Diagrams obtained after Q staining[10] and the patterns described are quite similar, but the diagrams shown here seem more distinct and detailed, implying that with the TL technique bands are better defined. Another advantage is that measurements can be made directly from the slide.

A possible future application of the technique will be automatic identification of the karyotype. A modified UMSP can be used for digital recording and thus a chromosome or a whole metaphase can be recorded and karyotyped by computer. Such studies are in progress.

Fig. 3 shows part of a digitally recorded metaphase which

has been converted manually to a diagram similar to that obtained with the technique described.

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Nuclear DNA Content Variability in *Xenopus laevis* : A Redundancy Regulation common to all Gene Families

IN an earlier communication[1] we presented data about the number (*R*) of redundant rRNA genes in somatic cells of several species of amphibians. We also determined the number (*A*) of extrachromosomal nucleoli produced during oogenesis by genetic amplification. Both *R* and *A* are constant for each species and vary among different species falling into categories following a geometrical progression (A and $R = 2^n$).

To account for these data and other known facts about rRNA genes, we proposed a model in which the behaviour of these genes during amplification is analogous to that of the genome of inducible viruses. During meiosis each rRNA gene of the nucleolar organizer is excised from the chromosome in the form of a circular monogenic DNA molecule. Each circle replicates, during the amplification phase, doubling its length at each replication round. After a number (*n*) of rounds, one of the amplified circles (containing the 2^n rRNA genes) is reintegrated into the chromosome to restore the lost cluster of redundant genes, while the others give rise to the extrachromosomal nucleoli. This model accounts for genetic rectification of the redundant rRNA genes: their homogeneity will be maintained without excluding the possibility of evolutionary changes in the whole family. One implication of this model is that the number of redundant rRNA genes is established anew at each meiosis by some kind of regulation.

Other genes known to be redundant are the 5S RNA[2], 4S RNA[2] and histone[3] genes, and it is to be expected that more redundant genes will be demonstrated, for a significant proportion of the eukaryotic genome is made up of repetitious DNA sequences[2]. Many years ago Callan[4] proposed that most if not all genes are redundant, on the basis of cytological observations. All these redundant genes would require an efficient mechanism of rectification such as the one we proposed for the rRNA gene family[1]. In this case, regulation would be necessary to establish the number of redundant genes of each family to be reintegrated into the genome. This regulation

Fig. 1 Hybridization of DNA prepared from $+/+$ *nu* and $+/p$ *nu* *Xenopus laevis* with rRNA (*a*), 5S RNA (*b*) and 4S RNA (*c*). DNA was extracted from livers of ten $+/+$ *nu* (A–J) and thirteen $+/p$ *nu* (K–W) animals selected as described in Table 1 among the progeny of two normal parents $(+/+$ *nu*). DNA extracted as previously described[1] was further purified on preparative CsCl density gradients. ^{3}H-labelled rRNA, 5S RNA and 4S RNA were obtained from a *Xenopus* cell line. Method of culture, labelling conditions, purification of rRNA by sucrose gradients and of 5S RNA and 4S RNA by 'Sephadex' columns have been described[7,8]. Molecular hybridization was carried out in triplicate at saturating conditions in $2 \times$ SSC at $65°$ C for 16 h at a ^{3}H-RNA concentration of 3 µg ml.[−1] (rRNA), 1 µg ml.[−1] (5S RNA), 3 µg ml.[−1] (4S RNA) as described[1]. After the filters had been counted, the amount of DNA retained on them was assayed[9]. Saturation levels are given as % of the average value obtained for $+/+$ *nu* animals.

Hybridized RNA–DNA (% of average $+/+nu$)
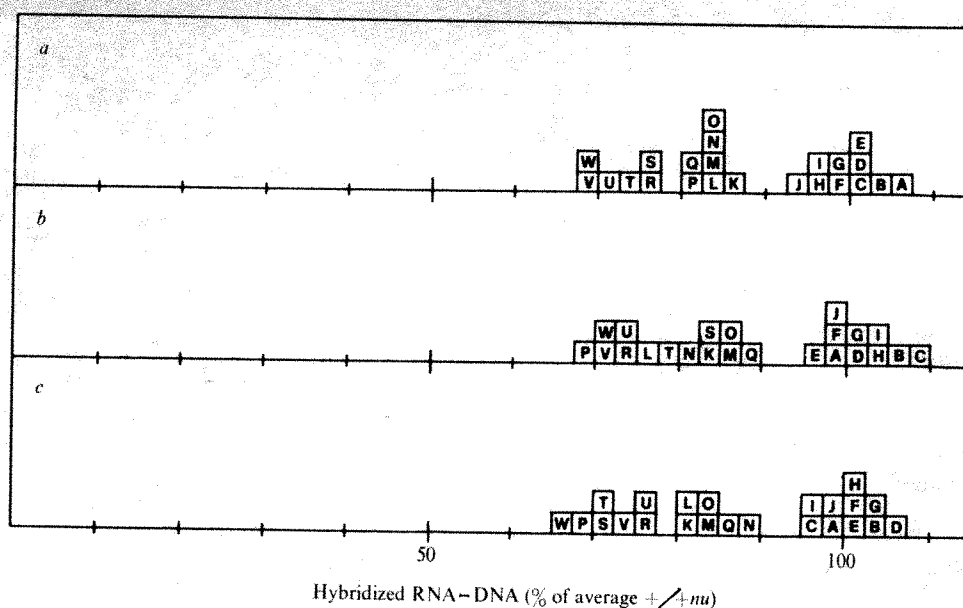
can either be independent for each gene family or, more simply, common to all of them. This can easily be tested: animals partially deficient in rRNA genes $(+/p$ *nu*) are frequently found in natural populations of *Xenopus laevis*[5]. According to our model this condition does not arise from a classical deletion but rather from an alteration of the regulation mechanism. If the hypothesis of a common regulation of redundant gene families were correct, we should expect a parallel decrease of the redundancy number of all gene families: this could be tested by measuring the DNA content of somatic diploid cells or titrating, by RNA-DNA hybridization, gene families other than rRNA—for example 4S RNA and 5S RNA gene families.

Table 1 summarizes the data on total DNA content measured by two different techniques. Individuals of $+/+$ *nu* and $+/p$ *nu* genotype were selected on the basis of different nucleolar sizes by phase contrast observation of somatic cells[5] (all partially defective individuals were classified as $+/p$ *nu* without attempting to distinguish the *p nu* from the *p^1 nu* condition[5]. All the $+/p$ *nu* animals show a decrease in total DNA content per diploid cell (a reduction of rRNA genes only would have affected the total DNA content of less than 0.1%) (Table 1). This decrease is not the same for all the $+/p$ *nu* individuals, which seem to fall into discrete categories. A first group of $+/p$ *nu* has a total DNA content around 5.25 pg/diploid cell. A second category has about 4.95 and a third about 4.75 pg/ diploid cell. The difference between the normal value $(+/+$ *nu*) and the first $+/p$ *nu* group is about double the difference between the first and second $+/p$ *nu* groups and about four times higher than that between the second and the third categories $+/p$ *nu*, suggesting that the size of gene families is progressively reduced to one half, one quarter or one eighth of normal. From these observed decreases (about 12%, 17% and 20% for the three categories respectively) of the total DNA content per diploid cell in $+/p$ *nu* animals it can be estimated that about 45–50% of the genome of *Xenopus laevis* is made up of gene families the redundancy of which is under common regulation. This finding is in good agreement with the known fact that about 50% of the genome of *Xenopus laevis* is made up of repetitious DNA sequences[6].

Alternatively, we used DNA from $+/+$ *nu* and $+/p$ *nu* *Xenopus laevis* for molecular hybridization experiments to measure the redundancy of 5S RNA and 4S RNA genes. Fig. 1 summarizes all data obtained hybridizing at saturation DNA separately extracted from 10 $+/+$ *nu* and 13 $+/p$ *nu* individuals with ^{3}H-labelled 5S RNA, 4S RNA and, as control,

rRNA (28S + 18S). As expected, the saturation level for rRNA (Fig. 1a) is reduced for all $+/p$ *nu* DNA with respect to the normal $+/+$ *nu*. A parallel reduction was observed for 5S

Table 1 DNA Content (pg/Diploid Cell) in $+/+$ *nu* and $+/p$ *nu* *Xenopus laevis*

	Indole		Feulgen histophotometry		Average	
	Individual No.	DNA pg/ diploid cell	Individual No.	DNA pg/ diploid cell	DNA pg/ diploid cell	DNA %
$+/+$ *nu*	1	6.02 ± 0.09				
	2	6.00 ± 0.06				
	3	5.96 ± 0.07				
	4	5.95 ± 0.08	*	5.95	5.95	100
	5	5.90 ± 0.10				
	6	5.87 ± 0.07				
$+/p$ *nu*	7	5.34 ± 0.08	13	5.28 ± 0.06		
	8	5.29 ± 0.05	8	5.23 ± 0.04	5.24	88
	9	5.25 ± 0.07	14	5.23 ± 0.07		
	10	5.17 ± 0.07	7	5.15 ± 0.11		
	11	4.96 ± 0.07	15	4.99 ± 0.05		
			16	4.95 ± 0.05	4.95	83
			17	4.94 ± 0.07		
			18	4.92 ± 0.06		
	12	4.77 ± 0.08	19	4.75 ± 0.09		
			12	4.71 ± 0.08	4.73	80
			20	4.70 ± 0.05		

$+/+$ *nu* and $+/p$ *nu* animals were selected by phase contrast microscope observation of squashes of buccal mucosa of adult animals from a natural population (1–12). Alternatively selection was done among tadpoles obtained crossing two normal $(+/+$ *nu*) parents, by examination of squash preparations of the tailtips; the tadpoles were then reared up to about 4 months after metamorphosis and checked again before use (13–20). At least ten DNA determinations for each animal were carried out on carefully counted samples of erythrocytes by the indole-spectrophotometric method as previously described[1]. Alternatively two blood drops from a $+/+$ *nu** and a $+/p$ *nu* animal were smeared side by side on the same slide, postfixed with methanol and Feulgen stained after 6 min 1 N HCl hydrolysis at $60°$ C. DNA measurement was carried out with a Leitz histophotometer on at least fifty nuclei of each individual. Comparison was always made between the $+/+$ *nu** and the $+/p$ *nu* sample on the same slide normalizing the result taking the $+/+$ *nu* equal to 5.95 pg/diploid cell (this value is the average obtained with the indole method for $+/+$ *nu* animals). In general the indole method was utilized with adult individuals from a natural population and the histophotometric method with those reared in the laboratory; individuals 7, 8 and 12 have been analysed by both methods. Standard deviation of the mean is given.

RNA and 4S RNA (Fig. 1*b* and *c*). As with the total DNA content, at least a first level of reduction is detectable at about 85% of normal in spite of obvious variability owing to technique and to the small number of animals tested. Lower levels, indistinguishable from each other, tend to approach about 65% of normal.

Saturation levels in Fig. 1*a*, *b* and *c* refer to a fixed amount of DNA; to obtain an estimate of the number of genes, these values must be corrected for the DNA content of diploid cells which, as previously mentioned, is different in +/+ *nu* and +/*p nu* individuals. For example the 85% saturation level, after correction for 5.25 pg/diploid cell DNA content, becomes about 75% of the 100% saturation level corrected for 5.96 pg/diploid cell DNA content. Lower levels tend to approach, after similar correction, a 50% value. This is just what we expect for a reduction of the redundancy of the three gene families analysed to 50%, 25% and so on, with respect to +/+ *nu*, considering that the *p nu* condition was carried on only one of the two chromosomal sets.

Our findings lead us to envisage an uninemic eukaryotic chromosome the DNA sequences of which can be distinguished in a backbone along which, at fixed loci, redundant genes are inserted. Non-redundant genes can also be present, as with globin genes[10,11]. Meiosis, that is the amplification phase, would present the opportunity for both redundancy regulation and genetic rectification of gene families. Although gene families share a common regulatory mechanism for redundancy, the absolute number of genes is not necessarily the same for all of them. Occasional changes of the redundancy regulation would cause all gene families to be numerically reduced to one half, one quarter and so on of the normal redundancy value. All these events might be explained by a process involving excision and reinsertion of redundant genes from the backbone in analogy with the model we proposed for rRNA genes[1]. Although a more detailed interpretation of these events is at present impossible, the analogy between redundant genes and episomes is suggestive.

The *p nu* condition, up to now thought to involve only the nucleolar organizer, involves in effect most if not all families of redundant genes. The size reduction of the nucleolus would be only a phenotypic aspect useful for the selection of these "low-redundancy" individuals.

We are reluctant to consider this condition in terms of mutation of a single redundancy regulator gene; in fact individuals with unequal sized nucleoli are found very frequently not only in natural populations but also among the progeny of normal individuals (+/+ *nu* × +/+ *nu*). Moreover in this last case the frequency is variable[5] from one to another cross: we have observed variability from less than 1% up to, in some cases, 30%.

We give a different interpretation to the anucleolate condition (*O nu*), which should be considered in terms of a deletion of the reintegration site for rRNA genes not affecting the redundancy of other gene families; in fact it has been shown[8] that these individuals have a normal number of 5S and 4S RNA genes. In agreement with this observation the only one +/*O nu* animal we could find had a normal DNA content per diploid cell.

We thank Mrs V. Auturori-Pezzoli and Mr A. Di Francesco, Mr F. Pasquetti and Mr G. Scotti for technical assistance. P. A. L.-S. is on leave from the Facultad de Medicina, Universidad Central de Venezuela, Caracas.

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Latimeria chalumnae: Reproduction and Conservation

Schultze[1] and Anthony and Millot[2] have concluded that the coelacanth, *Latimeria chalumnae*, is oviparous. Because of the general interest surrounding this species and considering the implications which modes of reproduction have on proposals for the conservation of *Latimeria*[2], we believe that a reconsideration of the reproductive mode in coelacanths is in order.

Schultze's arguments for oviparity in *Latimeria* depend on palaeontological data. Yolk sac larvae of the Carboniferous genus *Rhabdoderma* have been described, strong evidence that this particular coelacanth was oviparous. It was noted that neither fossil nor recent coelacanths possess modifications of the anal or pelvic fins for internal fertilization. Internal fertilization would, of course, be necessary for ovoviviparity or viviparity. Schultze further questioned the interpretation of Watson[3] that the occurrence of young *Holophagus* (*Undina*) inside a large specimen was evidence of viviparity in this Jurassic fossil, suggesting instead that this form was cannabalistic. The evidence presented by Anthony and Millot related to the enormous size of eggs removed from a recently-caught mature female *Latimeria* (8.5–9.0 cm diameter). They concluded that such large eggs were inconsistent with viviparity.

We agree that this evidence makes the occurrence of viviparity in *Latimeria* unlikely, but we feel that there is a strong possibility that the living coelacanth is ovoviviparous, providing an ample supply of nourishment prior to fertilization but maintaining the embryo internally during early development. Evidence in favour of ovoviviparity comes from physiological, morphological and palaeontological sources.

Latimeria retains high levels of urea to maintain its blood osmolality near that of seawater[4,5]. Viviparity, ovoviviparity, or the existence of a cleidoic egg are necessary concomitants of urea retention in Chondriichthyes, the only other major group to use the retention of urea for osmoregulatory purposes[4,6,7]. There is no evidence that *Latimeria* has a section of the oviduct modified for the production of egg membranes and cases necessary for the deposition of cleidoic eggs[2]. Embryonic elasmobranchs do not develop the capacity for renal and extrarenal retention of urea until late in development[7] which makes a protected foetal environment necessary. In oviparous forms the egg case and membranes restrict the loss of urea until the embryo is capable of urea production[8], and ovoviviparous and viviparous species provide a constant embryonic milieu through maternal urea production.

Morphological adaptations to ovoviviparity would necessarily include some means of internal fertilization. *Latimeria* lacks pelvic claspers or an anal fin specialized as an intromittent organ (indeed the role of the latter in locomotion[9] would seem to preclude such specializations), but males do possess modi-

fications of the cloacal region[10,11], which are possibly develop-
ments for internal fertilization. These are the extension of the
cloaca into a tubercle, and a series of surrounding erectile
caruncules. In some teleosts and all tetrapods which have
internal fertilization the intromittent organ originates from the
cloacal region rather than from fins or limbs.

The palaeontological data are not inconsistent with our hypo-
thesis of ovoviviparity in coelacanths. We feel that Watson's[3]
arguments in favour of the proposition that young *Holophagus*
were undergoing development rather than digestion within the
large specimen are convincing although not completely con-
clusive. Although we admit that Schultze's interpretation that
Rhabdoderma was oviparous is probably justified, we note that
this species was at least partially of freshwater habitat and
both *Holophagus* and *Latimeria* seem to have been exclusively
marine[12]. In elasmobranchs urea retention is a specific
adaptation to marine environments that is abandoned in groups
such as the family Potamotrygonidae which are restricted to
freshwater[13-15]. *Rhabdoderma* probably did not retain high
levels of urea and its embryos would not have required a
protected environment. (It is possible, but not likely, that
Rhabdoderma was ovoviviparous and the yolk sac larvae
described by Schultze were released prematurely from a dead
or dying female.) The genus did possess large eggs (15–16 mm
in diameter[1]) which could be regarded as either a "preadapta-
tion" to or relic of ovoviviparity. Finally, we note that the
very size of *Latimeria* eggs is a strong argument that this
species has a high degree of parental care, involving either
ovoviviparity or guarding a cluster of eggs. It is difficult to
believe that *Latimeria* could survive at all unless the small
number of eggs were protected from predation.

Our discussion has pointed to the possibility that *Latimeria*
is ovoviviparous. That a question still exists regarding the
mode of reproduction in this fish indicates the need for a regular
collection of data (presumably by the officials in the Comoro
Islands responsible for the preparation and distribution of
specimens) on sex, reproductive state, and possible occurrence
of embryos of coelacanths caught in the future. Few of the
more than 70 caught have been dissected and the sex of many
has not been recorded (20 females and 25 males have been
reported[16]). Another step which might be taken is to check
the specimens which have already been caught and sent to
various universities and museums for reproductive condition.
We understand the reluctance of museums to dissect exhibition
specimens, but the surgery involved would involve only a
minor extension of the incision routinely made in the Comoro
Islands, and the discovery of embryos would greatly enhance
both the scientific and popular value of the fish. Fortunately,
the officials in the Comores have maintained records of the
dates, depths, and sites of capture for each specimen and it
should be possible to reconstruct any seasonal or migrational
pattern in the reproduction of *Latimeria*.

We share the concern of Anthony and Millot[2] for the
protection of *Latimeria*, but we feel that their proposal for a
ban on coelacanth fishing from December 15 to March 15 is
premature until more is known of the reproductive biology and
population levels of the fish. Male *Latimeria* are seemingly
in active spermatogenesis from September until February[17]
and large eggs have been reported in January, which suggests
that breeding occurs somewhere between November and
February. If coelacanths are oviparous and do not guard a
cluster of eggs the December to March interdiction proposed
by Anthony and Millot might be justified. If, on the other
hand, *Latimeria* is ovoviviparous, the time during which the
embryos are maintained inside the mother (which could extend
for many months as in elasmobranchs) would be the phase
most deserving of protection.

We are not, however, fully convinced that the present fishery
for coelacanths represents a serious threat to the survival of
the species. Aside from the initial specimen from South Africa,
all known coelacanths have been caught in the Comoro
Islands by native fishermen using the same techniques and

equipment which they have been using for many centuries.
The natives do not normally fish specifically for coelacanths
but catch them while seeking other species, principally the
oilfish, *Ruvettus pretiosus*. The reward offered by the govern-
ment, while generous, does not provide a sufficient incentive to
justify a deliberate fishing effort for *Latimeria*, which is un-
commonly caught. Whether the infrequency with which
coelacanths appear (some 3–4 per year) is due to rarity, to the
inaccessibility of their habitat, or to inefficiency of native
fishing is uncertain. From records kept by Comorean officials
there seems to be no change in the catch rate of coelacanths
caught over the years in which such data were collected. This
suggests to us that the population is relatively stable.

The observation that *Latimeria* is relatively common at
only a few sites within the Comores[2] could be due to sampling
error rather than a real population distribution. The areas
from which most coelacanths have been reported (the west
coasts of Grande Comore and Anjouan) include large fishing
villages in which a substantial night fishery for *Ruvettus* occurs.
Other regions in the Comores may well lack the concentrated
fisheries which occur in these areas. Indeed, the restriction of
Ruvettus longline fisheries to the Comoro, Society and Cook
island groups[18] may well be the principal reason that, with
the exception of the initial South African record, *Latimeria*
is known only from the Comores.

We are not convinced that *Latimeria* is currently in danger
of extinction, but we feel that studies to determine the popula-
tion level of this fish in the Comores are critical for the
establishment of a sound policy of conservation which would
both protect *Latimeria* from possible overfishing and preserve
the livelihood of the native fishermen. Such studies could
include a survey of *Latimeria* habitats utilizing submersibles,
remote television and photography. The possibility of tagging-
recapture studies might also be considered after it has been
determined what factors are responsible for the limited ability
of *Latimeria* to survive in surface waters[9,19,20]. If feasible,
such studies could provide data on growth, migrational patterns,
and population density while harming neither the *Latimeria*
population nor the native economy.

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CORRESPONDENCE

Science and Politics

SIR,—The discussions about Tel Aviv, Vietnam, politics and parish of *Nature*, including the latest ones by Drs Simonen (*Nature*, **241**, 487 ; 1973), Lloyd (*Nature*, **242**, 213 ; 1973) and Rognes (*Nature*, **242**, 143 ; 1973), must ultimately deal with the questions of how scientifically advanced nations have used science and technology politically and militarily to repress the peoples of scientifically less developed countries, and to what extent science and scientists in the more developed countries are responsible for that effect.

It is difficult to find any period, since the time of Francis Bacon, when science was not employed for, or benefited by, repression and exploitation, mainly by Europeans (later joined by Japanese) against other peoples of the world, the Vietnam war being just the latest example. It is remarkable that, during the past, such a repression was accepted by the scientific community almost without a stir. If Dr Lloyd talks about the politics of the 1930s, let us remember what state the indigenous people of Asia, Africa and Oceania and the non-European people of America were then in, and that colonial European powers as well as the United States and Japan then benefited themselves from that state, while Germany was excluded from it. Let us also remember that the "political nemesis of 1939" was precipitated by a culmination of the desperate struggle, both political and economic, among these nations for more benefit in this sense. Certainly Scandinavians were the least involved.

It is, therefore, really remarkable that through Vietnam scientific communities (mostly guided by younger members and students) have finally come to realize this stark reality and have begun to understand the role played by science during the last three centuries. Insofar as the discussion leads to a revelation of this point, the political arguments put forward by the previous correspondents were all in the thick of *Nature's* parish.

In this sense, preaching may be just as important as any other means to achieve a gradual liberation of scientists from the previously held delusions, at least for some time to come. If scientists all over the world realized that their competition for excellence within the rule of "objective" scientific enterprise is instrumental in the political and military control exercised on "subjective"

criteria, and if they could unite world-over to refuse lending their support to the military end, scientists could exert an influence on politics because politics today cannot operate without scientists. The effect of such actions would be significant only if they were staged simultaneously all over the world. To begin with, scientists in scientifically more advanced nations should learn to direct their attention to those who would suffer rather than benefit from science. However, as little research funding would come from such suffering people, it follows that little scientific research into these problems would be practised for some time. What else other than preaching, based on theories, is effective for even slowly breaking this dilemma?

Lastly, could we not count the emergence of a large number of independent non-European nations all over the world during the last 25 years as examples of successful political preaching?

Yours faithfully,

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Research Priorities

SIR,—Your copy of January 19 has just become available here. I was deeply dismayed to learn from your editorial (*Nature*, **241**, 153 ; 1973) of the many people (apart from astrophysicists) who are leading lives of discomfort for lack of a "better understanding of the difference between pulsating stars and other kinds of stars". Here, too, we have many people who are leading lives of discomfort, due to such things as malnutrition and malaria, bilharzia and river blindness. Research, such as a deepening of our understanding of the ecology of the vectors of disease, would probably fall into your category of trivial problems. Both these considerations now make it clear to me why, although it is possible to spend many millions of dollars or pounds upon research in radio astronomy, requests for far more modest assistance to develop research schools in Africa upon the trivial problems falls largely upon deaf ears.

It is my sincere hope that the astronomers will soon solve this problem about pulsating stars and other kinds of stars, not only so that the people of the United Kingdom and the United

States "will find the Universe a more comfortable place in which to live", but also because it might then be possible to spare some research funds in the interests of people with a narrow vista and who would be content if we could make just the world a more comfortable place for them.

Yours faithfully,

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Psychiatric Decisions

SIR,—Szasz (*Nature*, **242**, 305 ; 1973) continues to raise very important issues demonstrating the arbitrary nature of many psychiatric decisions, and the power society invests in psychiatry. He also raises anxieties, however, by his dogmatic response to imponderable questions.

"Ill", for example, is a word meaning different things in different sentences. It is not necessarily stretching it too far, for example, when describing a woman, aged 26, who after the birth of her child seems intent on suicide and slaughter. Yet Szasz seems to imply that she should be allowed to kill herself without medical intervention, and for killing the child she should go to prison *via* the courts.

I personally believe that many philosophical problems about freedom, illness, and responsibility are outrageously neglected by naive practical psychiatrists. Like many physicians, psychologists and scientists, they are for common sense, and spurn philosophizing as irrelevant hot air. Indeed its only advantage is to show how like an artist the complete physician must be. He must make decisions while thinking in a necessarily inadequate language.

The total impact of what a psychiatrist does is what is important. Szasz rightly challenges a simple view, but in remaining human and avoiding where possible coercion, occasionally a psychiatrist is being a better physician by having the courage to use compulsion in the interest of his patient.

Yours faithfully,

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Announcements

University News

Professor **Jack Tizard,** University of London, Institute of Education, has been awarded the **Research Award of the American Association on Mental Deficiency** for 1973.

Miscellaneous

Dr G. F. Vaughan, Reading, has been appointed to the **Medical Research Council** as successor to Mr Laurence Pavitt.

Erratum

IN the article "Rapid Determination of Very Low Nitrogen Levels in Water" by S. F. Bankert, S. D. Bloom and F. S. Dietrich (*Nature*, **242**, 270; 1973) the expression p.p.b. was incorrectly converted during editing to 10^{-9} g kg^{-1} and should read 10^{-6} g kg^{-1} throughout.

International Meetings

May 4–5, Sargassum Meetings (Dr E. B. G. Jones, Department of Biological Sciences, King Henry I Street, Portsmouth Polytechnic, Portsmouth).

May 15, The Results of the Spacecraft Missions to Mars (Executive Secretary, The Royal Society, 6 Carlton House Terrace, London SW1).

May 17, On Buoyancy and the Lives of Modern and Fossil Cephalopods (Executive Secretary, The Royal Society, 6 Carlton House Terrace, London SW1).

May 24–25, Structure and Function of Biological Membranes and Envelopes (Executive Secretary, The Royal Society, 6 Carlton House Terrace, London SW1).

May 30–31, Symposium on Field Instrumentation (Secretariat, IEE Conference Department, Savoy Place, London WC2).

May 31, The Value of Automation in the Health Service (Executive Secretary, The Royal Society, 6 Carlton House Terrace, London SW1).

June 3–8, 2nd Congress—International Society of Aesthetic Plastic Surgery (The Secretariat, PO Box 16271, Tel Aviv, Israel).

June 4–7, 1st International Symposium on Environmental Mutagens (Dr B. J. Kilbey, Department of Genetics, University of Edinburgh, Scotland).

June 4–7, 24th Annual Meeting of the Tissue Culture Association (Local Committee Chairman, Dr George Yerganian, Children's Cancer Research Foundation, 35 Binney Street, Boston, Massachusetts 02115, USA).

June 4–8, Radioimmunoassay and Related Procedures in Clinical Medicine Research (Dr E. J. Garcia, International Atomic Energy Agency, Kärtner Ring 11–13, A1010 Vienna, Austria).

June 4–8, International Marine and Shipping Conference (The Institute of Marine Engineers, 76 Mark Lane, London EC3R 7JN).

June 4–8, 5th Congress of the International Ergonomics Association (Organisatie Bureau Amsterdam NV, Postbus 7205, Amsterdam, The Netherlands).

June 4–8, 2nd World Congress on Ultrasonics in Medicine (Secretariat, 2nd World Congress on Ultrasonics in Medicine, Holland Organizing Centre, 16 Lange Voorhout, The Hague, The Netherlands).

June 4–8, The Treatment of Malignant Lymphomas (Miss Lucia Manfredi, Ufficio Attività Didattiche, Istituto Nazionale per lo Studio e la dei Tumori, Via G Venezian, 20133 Milano, Italy).

June 7–9, International Congress on Immunology (Professor N. Carretti, Obstetrics and Gynaecology Clinic, University of Padua, Via Giustiniani No. 3, Padua 35100, Italy).

June 11, Charge Transfer Devices (Meetings Officer, The Institute of Physics, 4 Belgrave Square, London SW1X 8QX).

June 11–13, Symposium on the Loch Leven IBP Project (Dr D. S. McLusky, IBP Loch Leven Symposium, Department of Biology, The University, Stirling FK9 4LA).

June 12, Data for Scientists and Technologists (Honorary Secretary, Mr D. F. Styles, 55 Penrhyn Avenue, Middleton, Manchester M24 1FP).

June 12–14, 27th Annual Frequency Control Symposium (Commander, US Army Electronic Command, Dr J. R. Vig, Fort Monmouth, New Jersey 07703, USA).

June 13, Techniques for the Investigation of Metal Failures (Meetings Secretary, The Institution of Metallurgists, Northway House, High Road, Whetstone, London N20 9LW).

June 13, Symposium on Mathematics in Management (Secretary and Registrar, The Institute of Mathematics, Maitland House, Warrior Square, Southend-on-Sea, Essex SS1 2JY).

June 13–15, International Conference on Hydrostatic Extrusion (Mr I. A. McNish, Department of Trade and Industry, Birniehill Institute, National Engineering Laboratory, East Kilbride, Glasgow).

June 13–15, 28th Annual Calorimetry Conference (James J. Christensen, Department of Chemical Engineering, 138 FELB, Brigham Young University, Provo, Utah 84601, USA).

June 17–21, 18th Annual Meeting of the Health Physics Society (Mr S. C. Bushong, Department of Radiology, Baylor College of Medicine, Houston, Texas 77025, USA).